DISSERTATION ON

STUDY OF TESTOSTERONE LEVELS IN MEN WITH TYPE 2 DIABETES MELLITUS

Submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the regulations
for the award of the degree of

M.D. BRANCH - I
GENERAL MEDICINE
MADRAS

CHENGALPATTU MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL, CHENGALPATTU

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA

APRIL 2013

CERTIFICATE

This is to certify that the dissertation entitled "**STUDY OF TESTOSTERONE LEVELS IN MEN WITH TYPE 2 DIABETES MELLITUS"** is a bonafide work done by Dr. P.ASIR JULIN, post graduate student, Department of Medicine, Chengalpattu Medical College and Government General Hospital, Chengalpattu in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I General Medicine, under my guidance and supervision, during the Academic period from April 2010 to April 2013.

Prof. K.E ARUMUGAM, M.D.,
Professor of Medicine,
Department of Medicine,
Chengalpattu Medical College,
Government General Hospital,
Chengalpattu.

Prof. P. R THENMOZHI VALLI, M.D.,
The Dean
Chengalpattu Medical College
Government General Hospital,
Chengalpattu.

DECLARATION

I solemnly declare that this dissertation entitled "**STUDY OF TESTOSTERONE LEVELS IN MEN WITH TYPE 2 DIABETES MELLITUS"** was done by me at Chengalpattu Medical College and Government General Hospital during 2010-2013 under the guidance and direct supervision of **Prof. K.E ARUMUGAM, M.D.,** Professor of Medicine, Department of Medicine, Chengalpattu Medical College and Government General Hospital, Chengalpattu. This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree in General Medicine (Branch-I).

Place: Chengalpattu **(DR. P.ASIR JULIN)**

Date:

ACKNOWLEDGEMENT

At the outset, I thank **Prof. P. R THENMOZHI VALLI, M.D.,** Dean, Chengalpattu Medical College and Government General Hospital, Chengalpattu for having permitted me to use the hospital data for the study.

I am very much thankful to **Prof. R. JEGANATHAN, M.D.,** Medical Superintendent, Chengalpattu Medical College and Government General Hospital, Chengalpattu for permitting me to carry out my study.

I am indebted to **Prof. K.E ARUMUGAM, M.D.,** Professor of Medicine, Department of Medicine, Chengalpattu Medical College and Government General Hospital, Chengalpattu, for his support and his painstaking efforts and guidance in scrutinizing the study.

I thank **Prof. VASUMATHI M.D.,** Professor of Medicine, Department of Medicine, Chengalpattu Medical College and Government General Hospital, Chengalpattu for her guidance throughout the study.

I thank **Dr. DHARMARAJ M.D., Dr. RAVI SHANKAR M.D.,** Assistant Professors of Medicine, Chengalpattu Medical College and Government General Hospital, Chengalpattu for their contributions to the study.

I thank all my professional colleagues for their support and valuable contributions and criticisms.

Last but not the least, I would wish to thank all the patients without whose kind cooperation, this study would not have been possible.

STUDY OF TESTOSTERONE LEVELS IN MEN WITH TYPE 2 DIABETES MELLITUS

ABSRACT

BACKGROUND

Diabetes Mellitus, one of the most common non- communicable diseases, is a chronic metabolic disorder which is heralded by a number of micro-vascular and macro-vascular complications which are well known of. But the other endocrinological perspective of diabetes is often not given much importance. Most diabetics are associated with low levels of testosterone. Yet this aspect is not often investigated mainly because hypotestosteronemia is usually attributed to the aging process rather than diabetes itself. Moreover the symptoms of hypotestosteronemia are mostly non-specific, further making the diagnosis more elusive. The purpose of our study is to bring forth this association between type 2 diabetes mellitus and hypotestosteronemia.

METHODOLOGY

We started the study with the selection of cases and controls. We selected 100 diabetic men from our Diabetology OPD, Chengalpattu Medical College who fitted into the inclusion criteria as our cases. As controls, we selected subjects without history of diabetes mellitus whose FBS was less than 126 mg/dl on two occasions, from our male Medical OPD. Anthropometric measurements like height, weight, waist and hip circumferences were measured and BMI and Waist Hip ratio were calculated. Total cholesterol was measured. Total testosterone in the early morning (8:00–10:00 AM) was measured using CLIA (Chemiluminescence enzyme immunoassay) method. The average serum testosterone levels were compared between the diabetic and non-diabetic men and was statistically

analysed. The diabetic patients were further grouped, based on the duration of diabetes, BMI, cholesterol levels and presence or absence of associated risk factor and analysed.

RESULT

It was observed that on comparing the average total testosterone level between the two groups, we found that, there was a significant decrease in the testosterone levels in the diabetics compared to that of the non-diabetics in each age group. We also found that as the age progress there is a steady decline in the serum levels of testosterone in both the groups. But the fall in the testosterone values is much more significant in the diabetics.

Statistical analysis was made and the P values were calculated by the student T- test. The association between the diabetic and non-diabetics in each age group was found to be significant with a P-value of <0.05. Thus the decrease in the serum level of testosterone is found to be significant.

As the second part of our study we compared the serum testosterone levels among the diabetic men, by separating them into smaller groups, using multiple parameters such as duration of diabetes, BMI, Waist Hip ratio, cholesterol levels, associated other risk factors. We were able to derive an inverse relation between serum testosterone levels and most of these parameters. Thus we also evaluated the effects of multiple risk factors on diabetic men and testosterone levels.

CONCLUSION

Thus, through this study we demonstrate the association between type 2 diabetes mellitus and testosterone. We conclude that, there is a significant reduction in the levels of serum testosterone in diabetic men as compared to that of non-diabetic men. Even though the declining trend of the testosterone levels occurs

as the age increases the reduction in the testosterone levels are more significant in the diabetic group as compared to that of the non-diabetic men. Thus from our study we propose that age factor alone is not the cause of hypotestosteronemia in diabetes men.

From the analyses of different factors like BMI, cholesterol and other risk factors we have shown the influence of multiple factors on the levels of testosterone. Thus, in diabetic patients, hypotestosteronemia is a common entity. We suggest the measurement of testosterone in patients with diabetes, as the replacement of testosterone can have multiple benefits in diabetic patient to prevent diabetic complication and cardiovascular diseases. Testosterone level can further predict the development of type 2 diabetes mellitus, the utilization of this aspect of testosterone in future, is not too far.

KEY WORDS

Type 2 diabetes mellitus, testosterone, and risk factors, BMI

CONTENTS

INTRODUCTION

Testosterone a 19-carbon steroid secreted by the testis (Leydig cells) is the primary circulating androgen in the male human. Testosterone is essential for health and well-being and its levels decreases with aging. Men with type 2 diabetes mellitus have low testosterone levels, but this concept has not received much attention because of the fact that both type 2 diabetes and hypotestosteronemia are associated with aging. But studies have shown that young men with type 2 diabetes mellitus do suffer from low testosterone levels.

Testosterone plays a vital role in the metabolism of glucose and lipid. Decreased levels of serum testosterone often have adverse effects on the metabolic profile. Epidemiological studies have shown that there is a direct relationship between the serum testosterone levels and insulin sensitivity, and that hypotestosteronemia is associated with an increased risk of type 2 diabetes mellitus. It is also found that there is an inverse correlation between serum testosterone and fasting insulin levels in men irrespective of age and obesity. The mitochondrial dysfunction is the key factor leading to insulin resistance in men.

Lower total testosterone and sex hormone-binding globulin (SHBG) predict a higher incidence of metabolic syndrome. There is evidence that

hypotestosteronemia should be an element in the definition of metabolic syndrome, since low levels of testosterone are associated with or predict the development of metabolic syndrome and of diabetes mellitus.

In men with decreased serum levels of testosterone and type 2 diabetes mellitus, C-reactive protein concentration have found to be decreased which leads to increased risk of developing atherosclerosis and coronary heart disease independent of the risk associated with diabetes mellitus alone.

Further testosterone replacement suggests that there is a shift of fat mass to lean body mass. Both the systolic and diastolic blood pressure reduced and the mean plasma glucose levels declined. There was a significant improvement in lipid profiles. There was also an initial significant decrease in levels of liver enzymes. Additionally, there was a marked reduction in the C-reactive protein levels.

Further perspective is the healing of the diabetic ulcers with testosterone replacement therapy and therefore the use of testosterone in recalcitrant ulcers.

AIMS & OBJECTIVES

- To evaluate the level of serum testosterone in men with type 2 Diabetes Mellitus and to compare it with that of non-diabetic men of the same age.
- Effect of multiple parameters like obesity, hypertension etc. on the serum testosterone levels in men with type 2 Diabetes Mellitus.

REVIEW OF LITERATURE

Though the effects of testosterone have been known since ancient times, it was Ernest Laqueur [1] who first used the term *testosterone* (T) in 1935 when he isolated it from the bull testes. It is derived from the German word *Testosteron* (1935), coined from a presumed combined form of L. *testis* "testicle" (*testis*) + *ster(ol)* (*steroid*) + chemical ending *-one*.[2]

HISTORICAL MILESTONES:

The researches done on testosterone dates back to the 1800 [3]. Since antiquity, medicine men and scientists had the knowledge that castration of the testes leads to the loss of the vitality of men and animals. A German physiologist, Arnold Berthold [4], in 1849 experimented with four roosters, where he removed the testes in two roosters and transplanted it into the abdominal cavity of the other two [5]. The castrated roosters became fat and lazy which is a sign of testosterone loss. The two with grafted testes remained a rooster with bright red combs. [6]

Ernest Laqueur received the Nobel Prize [7] in 1935 for isolating the testosterone molecule. It was found in 1951 that, testosterone will produce a positive nitrogen balance and can increase the lean muscle mass [8]. This forms the basis that testosterone can be useful in the treatment of cardiovascular

disease [9] by synthesis of protein. With positive nitrogen balance there is increased protein synthesis which leads to easy repair of the bodily structures when damaged [10]. In addition, testosterone also induces the production and synthesis of the protein enzymes which are useful for the structure and functioning of the organs.

It was in 1935 that the newer era of modern testosterone therapy began, when Aldolf Butenandt [11] and Leopold Ruzicka [12] synthesized testosterone chemically. Oral forms of testosterone were found ineffective and 17-alkylated derivatives of testosterone which was used orally became obsolete later due to its side effects. So other methods of testosterone delivery were tried. A buccal testosterone tablet [13] was introduced which adheres to the buccal mucosa and by dissolving slowly released testosterone. Implants of crystalline testosterone were also inserted in the subcutaneous tissue. The other form was as testosterone gels which were opted for its ease in application. During 1950 and 60's researches intensified to aid modifications in the testosterone preparations [14]. Orally effective T undecanoate was introduced during 1970's. Transdermal scrotal patches [15, 16] were invented in 1992. Non-scrotal transdermal patches [17] were accessible then in 2000. The most recent preparations used in testosterone replacement therapy are the injectable forms which includes testosterone enanthate, cypionate, and undecanoate [18].

Though we are very much aware of the association of type 1 diabetes mellitus with that of other endocrine disorders [19], that is the Polyglandular Autoimmune (PGA) Syndromes which includes adrenal insufficiency, type 1 diabetes mellitus, autoimmune thyroid disease, hypophysitis, celiac disease, atrophic gastritis, pernicious anemia, vitiligo, hypoparathyroidism, myasthenia and thymoma, the association of type 2 diabetes with other endocrinological abnormalities is not well established. Around early nineties studies involving the association between type 2 diabetes mellitus and hypotestosteronemia began.

Since 1960 researches were conducted on the role of testosterone on the cardiac well-being, its association with other cardiovascular risk factors and metabolic syndrome [20, 21]. The knowledge of low levels of serum testosterone as a reason for the all-cause mortality has led way to further researches. By many studies it is now proved that apart from attenuation of sexual symptoms testosterone supplementation also has other beneficial effect [22, 23].

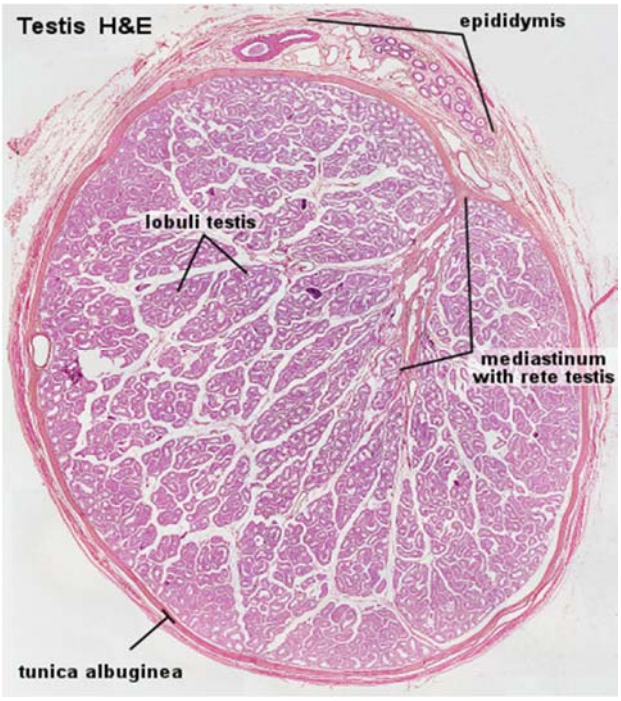
BACKGROUND:

Over the last few years, there have been several reports demonstrating that men with type 2 diabetes mellitus (T2DM) have a higher prevalence of hypotestosteronemia compared to that of normal population [24]. It has been found that reduced testosterone level is associated with increased risk of metabolic syndrome and diabetes [25]. In men, hypotestosteronemia has been observed to be associated with obesity, upper body fat distribution, and increased level of glucose and insulin [26]. Men with low serum testosterone levels present with loss of sexual interest, decreased vigor, depression, reduced bone strength, redistribution of body fat, easy fatigability. As these symptoms are usually non- specific, hypotestosteronemia is frequently under diagnosed [27]. Compared to normal population, individuals with hypertension, obesity, hyperlipidemia and diabetes have hypotestosteronemia [28, 29]. The purpose of this study, therefore, is to evaluate the serum level of testosterone in males with type 2 diabetes.

TESTOSTERONE:

Secretion:

The male gonad, testes secretes the male sex hormones, which are known as the *androgens* [30]. This includes *testosterone*, *dihydrotestosterone*, and *androstenedione*. Among these three hormones, testosterone is found to be secreted in larger quantities and so it is considered to be the important testicular hormone. It is to be noted that the testosterone eventually gets converted to dihydrotestosterone which then acts on the target tissues.

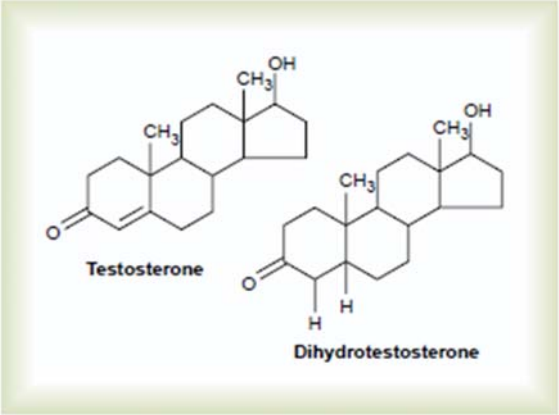


The *Interstitial cells of Leydig* [31], which are polyhedral cells that lies as clusters between the seminiferous tubules elaborates the hormone testosterone, and it is the main source of the hormone. The Leydig cells number and activity

parallel that of the testosterone surge. They are found to be more numerous in neonates in the initial months and then in the post pubertal adulthood period. In the childhood period these Leydig cell are scanty and so there is no detectable testosterone [32].

Chemistry [33]:

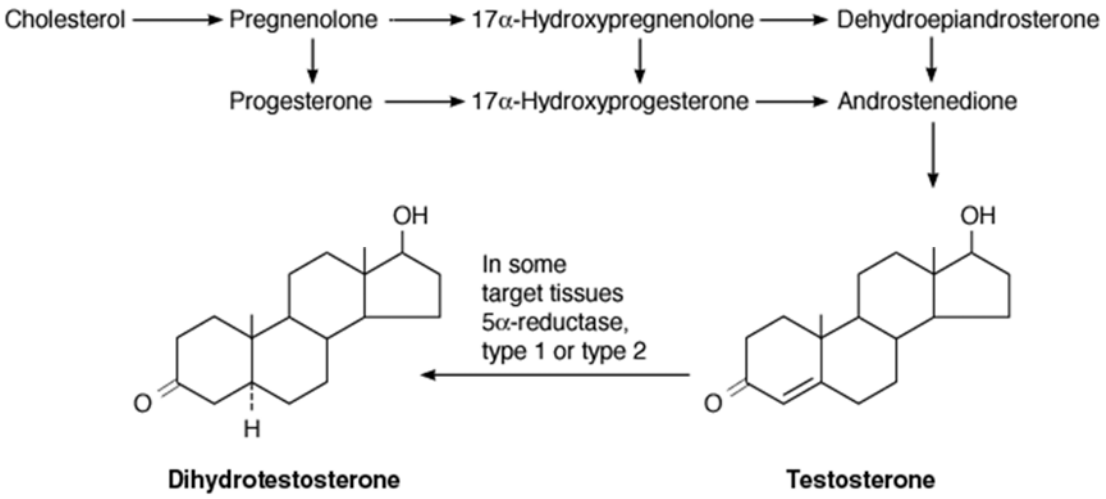
Testosterone, the principal testicular hormone is a steroidal compound, a C_{19} steroid with an -OH group in the 17 position. Its molecular formula being, C19H28O2.



Synthesis:

Testosterone is derived [34] from cholesterol, the major site of synthesis being the Leydig cells of the testes. Adrenal cortex also shares its contribution by the secretion of androstenedione which then gets further converted into testosterone. The rate limiting step in testicular steroidogenesis is the entry of

cholesterol into the mitochondria which need a transport protein. The initial step begins with the conversion of cholesterol to pregnenolone when it is acted upon by the side chain cleavage system. [35]. Pregnenolone is further converted into testosterone by two pathways, either by the progesterone pathway or by the dehydroepiandrosterone pathway. The array of enzymes which are involved includes 3 beta hydroxysteroid dehydrogenase, 17 alpha hydroxylase and 17, 20 lyase, 17 beta hydroxysteroid dehydrogenase. Reduction of the adrostenedione at the 17th carbon position results in the formation of testosterone.



Transport and Metabolism:

Testicular secretion of testosterone contributes to the major quantity of the testosterone in the circulation. It constitutes around 90-95%. The rest is contributed by the adrenal steroidogenesis and from the conversion of androstenedione to testosterone in the periphery [36]. The most important metabolic product of testosterone is dihydrotestosterone. It is mainly produced

peripherally from testosterone by a reaction that is catalyzed by the enzyme 5 alpha reductase, although the testes secrete a very minor quantity of dihydrotestosterone. In many tissues like the external genitalia, prostrate and some parts of the skin, dihydrotestosterone is the active form of the hormone. The production of dihydrotestosterone is around 400 micro grams as compared to about 5 grams of testosterone which shows that the plasma concentration of dihydrotestosterone is only one-tenth of that of testosterone concentration in adult males.

Testosterone gets metabolized by two pathways. The first pathway which involves oxidation is the major pathway. It occurs in many tissues including the liver and the end product being ketosteroids which are usually less active than testosterone. The second pathway involves reduction of the double bond and it occurs in the target tissues. The end product is dihydrotestosterone which is more potent than testosterone.

In male a small quantity of testosterone is converted into estradiol by peripheral aromatization and this contributes to about 80% of the circulating estradiol in men.

98% of the testosterone in the circulation is bound to protein the rest remains unbound as free hormone and it is this unbound free form which is biologically active. About 65% is bound to beta globulin also called the sex hormone–binding globulin SHBG [37] which has more affinity towards testosterone. The changes in the concentration of SHBG reflect upon in the

plasma level of testosterone. Conditions producing a decrease in SHBG are obesity, diabetes, administration of androgens, while aging and estrogen produces an increase. About 33% of the testosterone is bound to albumin.

The plasma testosterone level (free and bound) is 300-1000ng/dl in adult men and 30-70ng/dl in adult women.

Control of Testicular functions:

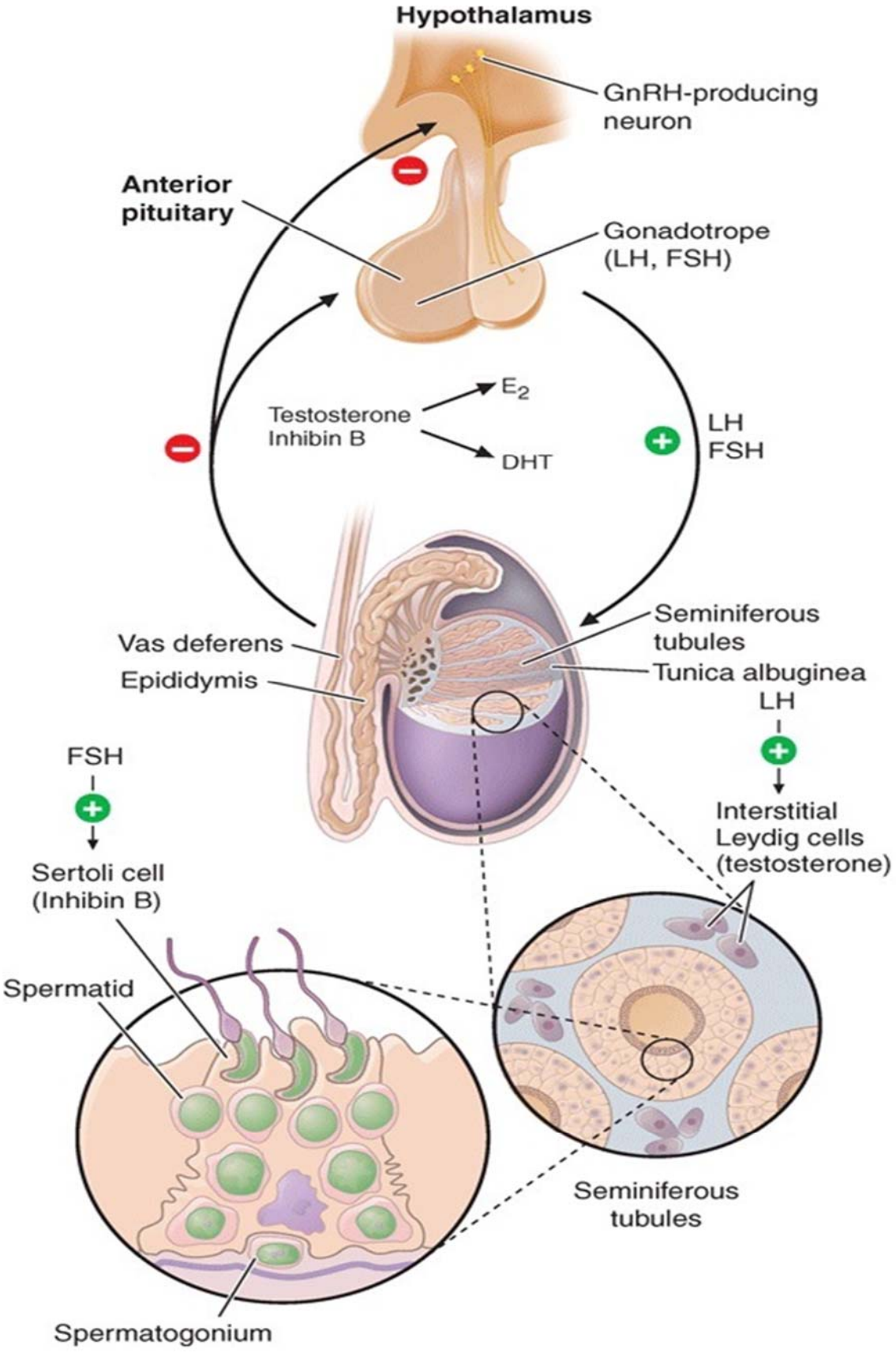
The secretion of testosterone is under the influence of the Luteinizing hormone (LH) secreted by the anterior pituitary. LH acts on the Leydig cells [38] and stimulates them to secrete testosterone. Excess testosterone in turn suppresses the secretion of LH from the pituitary. Testosterone does not have much influence on FSH (Follicle stimulating hormone) whereas another hormone called inhibin which is secreted by the Sertoli cells decreases the FSH concentration.

Steroid Feedback:

The current "working hypothesis" of the way the functions of the testes are regulated involves the feedback control of the LH on the Leydig cells and by FSH on the Sertoli cells. These in turn by the secretion of testosterone and inhibin controls the secretion of LH and FSH respectively. These feedback mechanisms are further under the control of GnRH secretion from the hypothalamus. It is to be noted that testosterone also has inhibitory control over

GnRH apart from LH. Castration is followed by a rise in the pituitary content and secretion of FSH and LH [39], and hypothalamic lesions prevent this rise. [40, 41]. Disorders involving the hypothalamus can lead to atrophy of the testes.

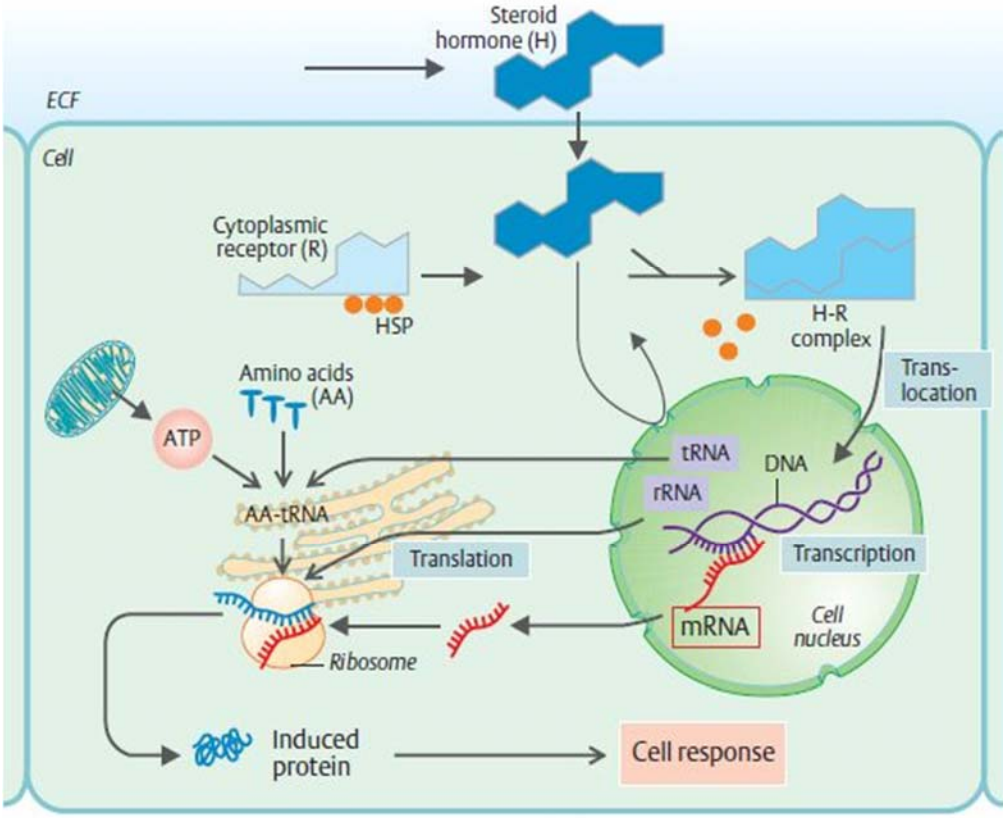
This hypothesis can be used upon clinically. Systemically administered testosterone has not found to increase the concentration of androgen in the local environment of the testes (a phenomenon which is necessary for normal spermatogenesis to occur i.e. increased concentration of androgens around the Sertoli cells) and this causes inhibition of LH secretion. Thus the ultimate effect of administering testosterone systemically is to produce a decreased sperm count. Thus is the use of testosterone as a method of contraception [42]. The main drawback is the need to use testosterone at very high doses, at with it produces side effects like sodium and water retention.


Hypothalamus
GnRH-producing neuron
Anterior pituitary
Gonadotrope (LH, FSH)
Testosterone
Inhibin B
E_2
DHT
LH
FSH
Vas deferens
Epididymis
Seminiferous tubules
Tunica albuginea
LH
Interstitial Leydig cells (testosterone)
FSH
Sertoli cell (Inhibin B)
Spermatid
Seminiferous tubules
Spermatogonium

Mechanism of Androgen Action [43]:

The androgen receptor (AR) [44] belongs to the superfamily of receptors which have highly conserved DNA binding domain in common-the nuclear receptor super family. The long arm of the X chromosome [45] codes for the androgen receptors.

Testosterone binds itself to an intracellular receptor and forms a receptor-steroid complex. This complex then binds to the DNA in the nucleus leading to transcription of various genes [46, 47]. Other mechanism of androgen action is through non-genomic mechanism.



Basic Intracellular Mechanism of Action of Testosterone

Most of the effects of testosterone result basically from an increased rate of protein formation in the target cells. This has been studied extensively in the prostate gland, one of the organs that is most affected by testosterone. In this gland, testosterone enters the prostatic cells within a few minutes after secretion. Then it is most often converted, under the influence of the intracellular enzyme 5 alpha-reductase [48], to *dihydrotestosterone*, and this in turn binds with a cytoplasmic "receptor protein" [49]. This combination migrates to the cell nucleus, where it binds with a nuclear protein and induces DNA-RNA transcription. Once the RNAP gets activated, the amounts of the RNA starts to rise, which then leads to a significant raise in the protein content of the cells [50]. After several days, the quantity of DNA in the prostate gland also increases and there is a simultaneous increase in the number of prostatic cells. Testosterone stimulates production of proteins virtually everywhere in the body, although more specifically affecting those proteins in "target" organs or tissues. Thus testosterone leads to the development of the primary sexual characteristics and those of secondary too. Recent studies suggest that testosterone, like other steroidal hormones, may also exert some rapid, non-genomic effects that do not require synthesis of new proteins. The physiological role of these non-genomic actions of testosterone, however, has yet to be determined.

Functions of Testosterone

In general, testosterone is responsible for the development of male body configuration. Even during fetal life, the testes are stimulated by chorionic gonadotropin from placenta to produce moderate quantities of testosterone throughout the entire period of fetal development and for 10 or more weeks after birth; thereafter, essentially no testosterone is produced during childhood until about the ages of 10 to 13 years. Under the influence of the luteinizing hormone from the anterior pituitary, the Leydig cells begin to secrete testosterone. This increase in testosterone starts with the beginning of puberty and continues secretion thereafter. As the age increases, the amount of testosterone secretion decreases, declining progressively after the age of 50yrs with the maximum fall being after the age of 80 yrs.

Functions of Testosterone during Fetal Development:

Testosterone begins to be elaborated by the male fetal testes at around seventh week of intra uterine life [51]. It can be said that, the main impetus for the development of a male fetus is the secretion of testosterone by the fetal gonads, which is mediated by the presence of the Y-chromosome. Testosterone also mediates the development of male internal genitalia and dihydrotestosterone (its active metabolite) mediates the development of the external genitalia. Those in which these impetuses are absent will develop into a

female fetus. By experimental studies it has been proved that when a large amount of testosterone is injected into a pregnant animal, even if the fetus was a female, it led to the development of male sex organs [52]. It was also found that when the testes were castrated early from a male fetus it developed female sex organs. These prove the essentiality of testosterone for the development of both the internal and the external genitalia in a male fetus [53] and at the same time it inhibits the development of female sex organs.

Effect of Testosterone to Cause Descent of the Testes. The testes usually descend into the scrotum during the 8^{th} to 9^{th} month [54] of gestation during which the testes begin secreting reasonable quantities of testosterone. If a male child is born with undescended but otherwise normal testes, injection of testosterone has been found to causes the descent of the testes normally. Administration of gonadotropic hormones also, which stimulate the Leydig cells of the newborn child's testes to produce testosterone, can also cause the testes to descend. Thus, the stimulus for descent of the testes is testosterone [55], indicating that testosterone is an important hormone for male sexual development during fetal life.

Functions of Testosterone after puberty:

Effect of Testosterone on Development of Adult Primary and Secondary Sexual Characteristics:

After puberty, the so long quiescent testes begin to secrete testosterone and the testosterone concentration increases considerably. This leads to certain changes in the external genitalia of the male i.e. enlargement of these organs. There is also enlargement of the prostate gland and the seminal vesicles with production of fructose by the seminal vesicles. The second important function of testosterone during puberty is the emergence of secondary sexual characteristics. These two are the very essential characters because it helps in distinguishing a man physically. Testosterone also enhances the male psychic effects.

Effect on the Distribution of Body Hair:

Testosterone causes the male pattern of hair growth over the body. These usually are present:

(1) On the beard area with the development of moustache

(2) Over the chest

(3) Over the abdomen along the linea alba up to the pubic symphysis

(4) Also on the back along the shoulders

(5) Pubic hair growth. It can also produce hair growth anywhere in the body but it generally decreases the scalp hair growth.

Baldness: As mentioned above, testosterone reduces the scalp hair growth especially on the crown of the head [56]; experimental studies have proved that castration of testes never produces baldness. But testosterone alone is not the

sole reason for baldness; it is the interplay of many factors especially genetic factors [57] followed by excessive androgens [58].

Effect on the Voice:

The masculine type of voice is a harsh and low pitched voice. This character to the voice is produced by testosterone. Testosterone makes the laryngeal mucosal hypertrophy with resultant laryngeal enlargement. Around puberty the voice become discordant initially which is termed "cracking" voice [59], this is followed by a gradual change to voice of an adult male.

Testosterone Increases Thickness of the Skin and contribute to Development of Acne:

Testosterone produces certain structural changes in the skin. Firstly it increases the skin thickness of the whole body and produces ruggedness of the tissues. Secondly it acts on the sebaceous glands and causes its growth and increases the secretion of sebum from the sebaceous glands. This results in the production of acne especially over the face [60]. Therefore, acne is a common feature of male adolescence when the body is first becoming introduced to increased testosterone. After several years of testosterone secretion, the skin normally adapts to it in a way that allows it to overcome the acne.

Testosterone Increases Protein Formation and Muscle Development [61]:

One of the most important male characteristics is the development of increasing musculature after puberty, averaging about a 50 per cent increase in muscle mass over that in the female. This is associated with increased protein formation in the non-muscular parts of the body as well. Many of the changes in the skin are due to deposition of proteins in the skin, and changes in the voice also result partly from this protein anabolic function of testosterone. Because of this great effect that testosterone and other androgens have on the body musculature, synthetic androgens are widely used by athletes to improve their muscular performance. This practice is to be severely deprecated because of the fact that prolonged harmful effects of excess androgens, in relation to sports physiology. Testosterone or synthetic androgens are also occasionally used in elderly age as a "youth hormone" to improve muscle strength and vigor, but with questionable results.

Testosterone Increases Bone Matrix and Causes Calcium Retention:

After the great increase in circulating testosterone which occurs during puberty (or after prolonged injection of testosterone), the bones grow considerably thicker [62] and deposit considerable additional calcium salts. Thus, testosterone increases the total amount of bone matrix [63] and causes calcium retention. The increase in bone matrix is believed to be a result of the general protein anabolic function of testosterone plus deposition of calcium salts in

response to the increased protein. Testosterone gives the male pelvis a differentiating effect from that of the female pelvis thereby making it strong to bear heavy weights. In the absence of testosterone, the male pelvis develops into a pelvis that is similar to that of the female. Because of the ability of testosterone to increase the size and strength of bones, as aging occurs it can lead to decreased BMD and it is often used in older men to treat osteoporosis [64]. When greater amounts of testosterone (or any other androgen) are secreted abnormally in the still-growing child, the rate of bone growth increases markedly, causing a spurt in total body height. However, the testosterone causes the epiphyses of the long bones to unite with the shafts of the bones at an early age. Therefore, despite the rapidity of growth, this early uniting of the epiphyses prevents the person from growing as tall. Even in normal men, the final adult height is slightly less than that which occurs in males are castrated before puberty.

Testosterone Increases Basal Metabolism [65]:

Injection of large quantities of testosterone increases the basal metabolic rate by as much as 15 per cent. This increased rate of metabolism is possibly an indirect result of the effect of testosterone on protein anabolism, the increased quantity of proteins—the enzymes especially—increasing the activities of almost all the cells.

Effect on Red Blood Cells:

When normal quantities of testosterone, is injected into a castrated adult, the number of red blood cells per cubic millimeter of blood increases by about 15 to 20 per cent [66]. Also, an average man has about 700,000 more red blood cells per cubic millimeter than an average woman. This difference is partly due to the increased metabolic rate that occurs after testosterone administration rather than to a direct effect of testosterone on red blood cell production.

Effect on Electrolyte and Water Balance:

Testosterone causes an increase in the distal tubular sodium reabsorption by the kidneys. Testosterone also has such an effect, but only to a minor degree when compared to that of the adrenal mineralocorticoids. Nevertheless, after puberty, the blood and extracellular fluid volumes of the males in relation to body weight increase as much as 5 to 10 per cent.

Normal Testosterone Levels in Men [67] by Age (Healthy)

Measurements in SI Units **(nmol/L)**			
Age	**Total Test**	**Free Test**	**SHBG**
25-34	21.38	0.428	35.5
35-44	23.14	0.356	40.1
45-54	21.02	0.314	44.6
55-64	19.49	0.288	45.5
65-74	18.15	0.239	48.7
75-84	16.32	0.207	51.0
85-100	13.05	0.186	65.9

Measurements in Conventional Units **(ng/dl)**, SHBG in (nmol/L)			
Age	**Total Test**	**Free Test**	**SHBG**
25-34	617	12.3	35.5
35-44	668	10.3	40.1
45-54	606	9.1	44.6
55-64	562	8.3	45.5
65-74	524	6.9	48.7
75-84	471	6.0	51.0
85-100	376	5.4	65.9

The normal testosterone level in young healthy males is between 300 and 1000ng/dl. Testosterone level shows diurnal variations with lower value in the afternoon.

CAUSES OF HYPOTESTOSTERONEMIA [68]

The causes of hypotestosteronemia are many to be enumerated. In a nutshell, there are three main levels at which defect can occur, finally leading to hypogonadism:

1. The level of the hypothalamus
2. The level of pituitary gland
3. The level of the testes.

When the defect lies in the hypothalamus or in the pituitary they are not able to produce appropriate quantities of gonadotrophins to stimulate adequate testicular secretions. Hence it is called hypogonadotrophic hypogonadism. When the testes are at defect though there are adequate quantities of gonadotrophins the testes is not able to secrete adequate amounts of testosterone. Hence it is called hypergonadotropic hypogonadism. In addition, SHBG also affects the serum testosterone levels.

- When the defect involve the gonads, the testes, then it is termed as "**primary hypogonadism or primary gonadal failure**[69] "
- When the pituitary gland or its control over testosterone regulation is at fault, it is termed as "**secondary hypogonadism** [69]," and

- When the defect lies high up in the hypothalamus, it is termed as "**tertiary hypogonadism** [69]." The last two entities are together called as hypogonadotrophic hypogonadism.

PRIMARY HYPOGONADISM OR PRIMARY GONADAL FAILURE (TESTES):

A. Primary gonadal failure may lead to defect in spermatogenesis, production and secretion of testosterone.
B. Chromosomal abnormalities**:** Klinefelter's syndrome [70], in which there is an abnormal testicular development with reduced size of the testicles ad decreased production of testosterone.
C. Anorchia syndrome [71]
D. Uncorrected cryptorchidism [72]
E. Acquired defects of the testes:
    1) Trauma to the scrotum resulting in testicular injury
    2) Torsion of testes leading to vascular insufficiency[73]
    3) Infections causing testicular damage (infectious orchitis):

- Viral orchitis may be caused by the mumps virus, group B arbovirus echovirus, lymphocytic choriomeningitis virus, most important of which is the mumps infection [74]
- Other bacterial and parasitic infections.

4) HIV infection[74]

5) Tuberculosis and Lepromatous leprosy

6) Toxic causes [75]

- *Drugs:* ketoconazole (inhibition of testosterone synthesis), spironolactone (blockade of androgen action), marijuana and digitalis (increased estrogen)
- Chemotherapeutic agent: causes direct inhibition of Cyclophosphamide,procarbazine and patients on MOPP (mechlorethamine, oncovin, procarbazine, prednisone
- Alcohol, when consumed in excess for prolonged periods, decreases testosterone, independent of liver disease or malnutrition.
- Known environmental hazards include microwaves and ultrasound and chemicals such as nematocide dibromochloropropane, cadmium, phthalates, and lead.

7) Systemic illness: cirrhosis, chronic renal failure, sickle cell anemia, acute febrile illness, celiac disease

8) Neurologic disorders: myotonic dystrophy [76], spinobulbar muscular atrophy, and paraplegia

9) Androgen Insensitivity Syndromes

10) **Aging [77]:** serum levels of testosterone declines with aging. But the available testosterone is still enough to carry out essential functions of the body.

11) **Hypotestosteronemia in women:** Certain conditions in women cause low levels of serum testosterone. These includes bilateral oophorectomy due to any gynecological cause and premature ovarian failure

SECONDARY AND TERTIARY HYPOGONADISM :

These are due to defect either at the level of the hypothalamus or the pituitary gland resulting in decreased production of the gonadotrophins (LH/ FSH/ GnRH) and failure of gonadal stimulation.

Some of the causes of hypogonadotrophic hypogonadism are:

1. Congenital Hypogonadotropic Disorders:

   Kallman's syndrome [78], *Laurence-Moon syndrome, adrenal hypoplasia congenital, Prader-Willi syndrome.*

2. Acquired Hypogonadotropic Disorders

- Tumors of the pituitary gland [79]
- Brain tumors
- Sellar Mass Lesions
- Tuberculosis
- Infiltrative diseases like hemochromatosis [80] sarcoidosis and histiocytosis X damages the pituitary gland
- HIV and AIDS [74] affects the hypothalamus and pituitary
- Anabolic steroid use
- Obesity [81]
- Hyperprolactinemia [83]
- Severe Illness
- Stress, Malnutrition
- Exercise

Normally, the conversion of testosterone to estrogen [82] occurs in the adipocytes. In the presence of obesity, the amount of fat tissue mass that can act as a site for this conversion increases and hence there is more aromatisation reaction taking place thereby, decreasing the serum level of testosterone, due to its excessive conversion in to estrogen in the adipocytes.

HYPOTESTOSTERONEMIA

DEFINITION [84]:

The American Association of Clinical Endocrinologists through detailed studies have come forward with the definition for hypogonadism which is defined as a serum level of testosterone <300ng/dl. [85, 86]. There is a diurnal variation in the level of testosterone. So it is better to measure the testosterone level in the morning rather than other timings i.e. around 8 a.m. in the morning [87, 88] In case the total testosterone levels are found to be subnormal before reporting it is always necessary to confirm it by a second test. Clinically there are certain indicators for the diagnosis of hypotestostreronemia, but most of these symptoms are non-specific. Hypotestostreronemia [89] is characterized by reduced sexual drive, reduced frequency of sexual intercourse or difficulty in maintaining erections, reduced growth of beard, loss of muscle mass, increased fat mass, decreased density of bone, decrease in testicular size, and enlargement of breast tissue. But only less than 10% of patients with erectile dysfunction alone have testosterone deficiency. Thus, it is always necessary to consider as a

whole, the entire symptomatology, to conclude as hypogonadism. Another lacuna in this area is that unless the symptoms are very profound it almost overlaps with the changes that occur in normal aging process.

TESTOSTERONE ASSAY:

When the word Total Testosterone (TT) is used, it means the measurement of both the bound form of testosterone as well as the unbound, free form. This total testosterone can be measured by a number of methods. Some of them are the radio-immuno assay method, liquid chromatography tandem mass spectrometry (LC-MS/MS) [90]. The more accurate method is the LC-MS/MS. This method is done by using organic solvents for the purpose of extracting the serum, followed by the isolation of testosterone from that of other steroids by the method of high-performance liquid chromatography and mass spectrometry, and finally to quantify the unique testosterone segments by mass spectrometry. The advantage of using this LC-MS/MS is that it is an accurate and a sensitive method for measuring even lower ranges of serum levels of testosterone. In future it is the method of choice for the estimation of serum levels of testosterone. Unlike many other hormone analyses, evaluation of testosterone levels can be accurate with the average testosterone levels with even a single sample but it must always be kept in mind that serum levels of testosterone fluctuate according to the pulsatile LH. When a patient presents with symptoms

consistent with hypogonadism, the initial step is the measurement of total testosterone in the morning sample using assay such as LC-MS/MS.

Measurement of Unbound Testosterone Levels [91, 92]

It is known that 98% of the plasma testosterone is bound to plasma proteins, either to sex hormone binding globulin (which carries most of the testosterone) or to albumin. The rest of the testosterone is called the unbound fraction or the free form. It should be noted that this form is the active form. This free form can be either calculated from the total testosterone levels and the sex hormone binding globulin by a formula called free androgen index in which ratio of total testosterone and the sex hormone binding globulin is obtained and expressed as percentage. Another method used for measurement of free testosterone is equilibrium dialysis method. Other method includes tracer analogue methods and though the results by this method are inaccurate it's a more convenient method. *Bioavailable testosterone* is the term used to indicate the unbound free testosterone plus testosterone which is bound loosely to the albumin; this b*ioavailable testosterone* is measured by the ammonium sulfate precipitation method. In elderly male and in patients in whom conditions associated with SHBG alterations are suggested, utilizing the equilibrium method for the direct measurement of free testosterone can be useful in unmasking testosterone deficiency

HCG Stimulation Test

There are two methods to perform an hCG stimulation test. [93] It can be performed either by administrating hCG as a single dose or as multiple doses and then recording the levels of testosterone. In the first method 1500–4000 IU of hCG is administered intramuscularly single dose. This is followed by measuring the level of serum testosterone at the baseline and then on 24, 48, 72, and 120 hours after injecting hCG. The second method is that of giving 1500 units of hCG on three successive days amounting to three hCG doses. Serum testosterone levels are analyzed at least 24 hours since the last dose. The expected response to this hCG stimulation test is that, in an adult male, there should be a doubling of the testosterone concentration. This test is of main purpose in children, especially prepubertal aged. A response of testosterone levels to >150 ng/dL in a prepubertal child shows that testicular tissue is present. When there is no response to this test, it shows that either the testicular tissue is absent or there is a functional defect in Leydig cells. Another test which is useful in the evaluation of undescended testes is the measurement of a substance called MIS, Mullerian inhibiting substance, secreted by the Sertoli cells in prepubertal boys [94].

LOW TESTOSTERONE IN TYPE 2 DIABETES

Men suffering from type 2 diabetes mellitus are found to have a low serum testosterone levels on comparison with men who do not have a previous history of diabetes mellitus. It has also been found that there exists an inverse relationship between serum testosterone and HbA1c concentrations [95]. A number of Meta-analytic studies have shown that there is a profound hypotestosteronemia in men with type 2 diabetes mellitus [96]. Conversely in men suffering from hypotestosteronemia the risk of developing type 2 diabetes mellitus is high. About 30-50% of the diabetic men have found to have associated hypotestosteronemia. Recent researches prove that testosterone replacement therapy has been found to be beneficial in men with low testosterone levels with associated type 2 diabetes mellitus or metabolic syndrome [97].

Experimental studies showed that testosterone has found to afford protection to the endothelium of the blood vessels thereby maintaining the integrity of the vasculature. Thus hypotestosteronemia leads to endothelial dysfunctions and its sequelae, irrespective of the presence of any other risk [98]. Further lower serum levels of testosterone concentrations can cause stiffness of the arteries in men suffering from type 2 diabetes mellitus [99]. This appears to be one of the main contributing factors for the development of cardiovascular risks in diabetic men.

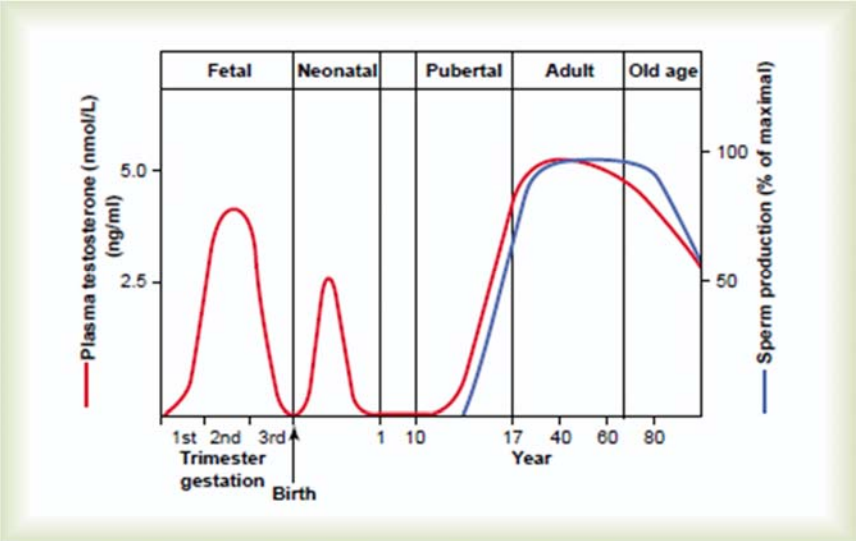
In men with type 2 diabetes mellitus presence of hypotestosteronemia is common entity but it still remains a hidden epidemic. This is in turn associated with insulin resistance. As the symptoms of hypogonadism are almost always nonspecific, it goes unnoticed unless profound. Some of the symptoms in diabetic men pointing towards testosterone deficiency include decreased libido, impaired mood, and low performance scale [100]. There appears to be a direct association between hypotestosteronemia and development of cardiovascular risk factors. Furthermore there are evidences suggestive of an inverse relationship between hypotestosteronemia and insulin resistance, which in turn is strongly associated with the development of complications of diabetes mellitus both micro vascular and macro vascular[101]. Prospective studies have proved that in patients with decreased levels of total testosterone (TT) who have associated insulin resistance there is a higher risk for the development of type 2 diabetes mellitus in future [102]. This is further proved by the fact that testosterone administration shows improvement in insulin sensitivity.

As it was explained previously, SHBG is the major transporter protein of testosterone in the circulation. Another important fact which must be kept in mind is that a low serum concentration of SHBG can by itself be associated with the risk of developing type 2 diabetes mellitus irrespective of whether serum testosterone concentration is decreased or within the normal ranges. [103] SHBG are found to be reduced in a number of critical illnesses in which

conditions it acts as a confounding factor. Estimation of the free testosterone values rather than the total testosterone would useful under such conditions [104].

The prevalence of hypogonadism is much more common than expected in patients with type 2 diabetes mellitus. This association is proved to be present independent of certain important factors such as the duration of diabetes, the status of the glycemic control, presence of micro or macro vascular complications and whether associated with other risk factor or not. Either alone or as a part of metabolic syndrome diabetes mellitus has a definitive association with diabetes mellitus.

Another important aspect in the evaluation of hypogonadism is aging. Testosterone concentration steadily declines after the age of 50 yrs. The total testosterone levels fall around 0.5 to 2% each year to reach a maximum fall around 80yrs. In diabetic patients there is a more profound decline in the testosterone concentration adjusted to age.



After analyzing a number of studies we are able to conclude that hypotestosteronemia is per se associated with an increase in all-cause mortality irrespective of whether associated with diabetes or metabolic syndrome [105]. Low testosterone levels associated with or without type 2 diabetes mellitus can be used as a predictor for the development of cardiovascular risks and complications irrespective of the presence or absence of other cardiovascular risk factors. Hypotestosteronemia and cardiovascular disease are associated with common risk factors like central obesity, redistribution of fat, inflammatory state and coagulation abnormalities [106]. Also in patients presenting with hypogonadism and cardiovascular disease (CVD) the mortality rate appears higher when compared to men without hypotestosteronemia [107].

Testosterone supplementation has been done to evaluate for the effects on the glycaemic status of men with type 2 diabetes mellitus and hypogonadism through many studies. But none of the studies has proven to give any conclusive results. Half of the studies showed no specific effect on the glycaemic status while half of the studies showed a definitive decrease in the glycaemic control with testosterone administration [108].

Testosterone and Insulin resistance:

Evidences from many data have proved that hypotestosteronemia is associated with the development of insulin resistance. A search into the actually

mechanism which leads to this resistance was made by many molecular studies of which the most convincing was the alterations in fatty acid metabolism, probably due to reduced expression of the genes which are necessary in oxidative metabolism. Similarly it has also been proved that testosterone improves the insulin sensitivity directly. Thus testosterone replacement has been found to increase the insulin sensitivity. Also it was found that in such men who were receiving testosterone supplementation for hypogonadism, when the treatment was stopped abruptly for around 15 days the insulin sensitivity decreased though without much alterations in the body composition. This is an evidence to show that testosterone has a direct control over sensitivity of insulin [109]. But some reports have shown that in elderly males by bringing the testosterone levels into normal range, there has been a favorable effects on the fat distribution and hence composition thus improving the insulin sensitivity, but they do not have any beneficial effect on the triglyceride metabolism [110]. But by experimental studies it has been proved that the effect of testosterone on insulin resistance was an acute phenomenon and the do not produce any immediate effect on the body composition. At the same time, experimentally, by reducing the estradiol concentration and by increasing the testosterone levels for a period of 7 days, it has reduced the insulin resistance with beneficial effects on the triglyceride metabolism, and has improved the postprandial glucose-dependent insulinotropic polypeptide (GIP) release [111]. Thus the association between testosterone, fat metabolism and obesity which by acting through a

common mechanism of increasing the proinflammatory factors, decreasing the insulin sensitivity thus produces endothelial dysfunction which are the essential factors leading to the development of cardiovascular diseases and erectile dysfunction (ED).

Pathogenesis of insulin resistance:

Present concepts throw light on the contributions of mitochondria in the pathogenesis of the development of insulin resistance. Studies on animal models have confirmed that, in insulin resistance there is a decreased expression of OXPHOS genes in skeletal muscle along with the down regulation of peroxisome proliferator–activated receptor-γ coactivator (PGC-1α) [112]. In proposing the model for demonstrating the pathogenesis of insulin resistance it was found that there was a reduction in the peroxisome proliferator–activated receptor-γ coactivator expression in the presence of physical inactivity in genetically susceptible subjects. The decreased expression of this single protein led to the decreased transcription of certain genes involved in the metabolism of fatty acids, leading to accumulation of triglycerides in the cells of the striated muscles, decreased expression of mitochondrial genes with the decreased efficacy of oxidative phosphorylation and resulting in insulin resistance ultimately. Experimental reproduction of hypogonadism has proved to show decreased oxidation of lipids and reduced BMR [113]. There is a positive relationship between the expression of the OXPHOS gene, VO_{2max} and the levels

of testosterone. There are not much data to explain the direct effect exerted by testosterone on insulin.

Another mechanism which is claimed in the development of insulin resistance is that of reduced glycogen synthetase activity [114] in experimental rats with low testosterone levels. This reduced activity of the glycogen synthetase [115] is computed to be the cause of the triglyceride accumulation in the myocytes intracellularly. The genetic model of type 2 diabetes mellitus with obesity is the Otsuka Long Evans Fatty (OLETF) [116] rat, confirms the effect of testosterone on the mitochondrial functions. These rats having low levels of androgens showed a decreased expression of peroxisome proliferator–activated receptor-γ coactivator and beta 3 receptor, androgen receptors present in the adipocytes. Further there is an increased expression of uncoupling protein 1 (UCP-1) and up regulation of its genes. All these lead to decreased peripheral utilization of energy, its accumulation as fats and therefore obesity [115]. When these OLETF rats were supplemented with testosterone (DHEA) for 2 weeks, it caused many positive effects in the form of improved insulin sensitivity, reduction of weight, decrease in FFA, and leptin concentration, all due to a considerable increase in the expression of UCP-1, β_3AR, and PGC-1α [116].

It requires further experimentations and analysis in to the expression of genes in the skeletal muscle with testosterone replacement. If the expression of the OXPHOS gene is found to be definitively modified by testosterone then

surely testosterone has a bright future in the prevention and treatment of type 2 diabetes mellitus in men with hypogonadism.

Testosterone and Metabolic syndrome:

Presently there have been many studies proving the correlation of metabolic syndrome and hypotestosteronemia. Such men have a reduced concentration of TT, FT, and SHBG [117]. This syndrome which includes an alteration in a number of metabolic parameters has an increased risk of mortality more so when the patient do have associated low levels of testosterone. There is a resulting proinflammatory state which leads to endothelial dysfunction and other complications like cardiovascular disease and ED. On the other hand, hypotestosteronemia can be used as a predictor for the future development of syndrome X and type 2 diabetes mellitus.

Low levels of serum total testosterone cause redistribution of fat and further accumulation of intra-abdominal fat thus leading to central obesity [118]. Independent of the age factor or the presence of obesity a low testosterone levels are associated with the development of metabolic syndrome. Experimentally suppression of testosterone in men caused an increase in the body fat [119]. The same effect occurs when there is a decrease in the concentration of sex hormone binding globulin. Since obesity is found to decrease the levels of both the sex hormone binding globulin and the total

testosterone SHBG is a confounding factor in defining the correlation between hypotestosteronemia and obesity [120].

There are a number of factors which determine the presence of hypotestosteronemia or low levels of sex hormone binding globulin. These include age, race, and obesity. But hypotestosteronemia is associated with type 2 diabetes mellitus independent of these factors or the diagnostic criteria of diabetes [121]. Studies also prove that TT, FT, and sex hormone binding globulin independently can be used in the prediction of the development of type 2 diabetes. [122] There is an emerging interest on SHBG as an independent positive predictor of diabetes mellitus. But some recent studies have proved that free testosterone cannot be useful for this purpose [124]. As mentioned above SHBG is a confounding factor for the association of hypotestosteronemia and type 2 diabetes mellitus and since most cases of diabetes are associated with obesity, obesity also remains confounding to establish this relationship. Compared to non-diabetic men reduced free testosterone concentrations are more prevalent in diabetic men [123]. Also, low SHBG was found to be a strong independent predictor of type 2 diabetes mellitus [124]. Finally, in prospective studies, androgen deprivation therapy either using bilateral orchidectomy or gonadotropin-releasing hormone agonist in older men with prostate cancer is associated with an increased risk of diabetes and CVD [125].

Pathobiology of low testosterone in type 2 diabetes

Adipocyte is biologically active tissue secreting a number of substances cytokines and chemokines. Some of them include adipokines, tumor necrosis factor (TNF)-α, interleukin (IL)-6, IL-1β, VEGF, transforming growth factors, plasminogen activator inhibitor-1, and angiotensinogen [126]. All of these factors are mediators in inflammation. Thus there is an inflammatory state which is set up in the body milieu. When the amount of the adipose tissue increases as it occurs in obesity, there is a chronic proinflammatory state set up in the body which results in increased concentration of inflammatory mediators as well as FFA and an increased estrogens output from the adipose tissue, which is obtained by its conversion from testosterone. This state of chronic inflammation leads to alteration in the blood mechanics with stiffness of the vasculature and endothelial dysfunction. All these together results in systemic inflammation and contributes to the development of metabolic syndrome and type 2 diabetes mellitus as well as hypotestosteronemia.

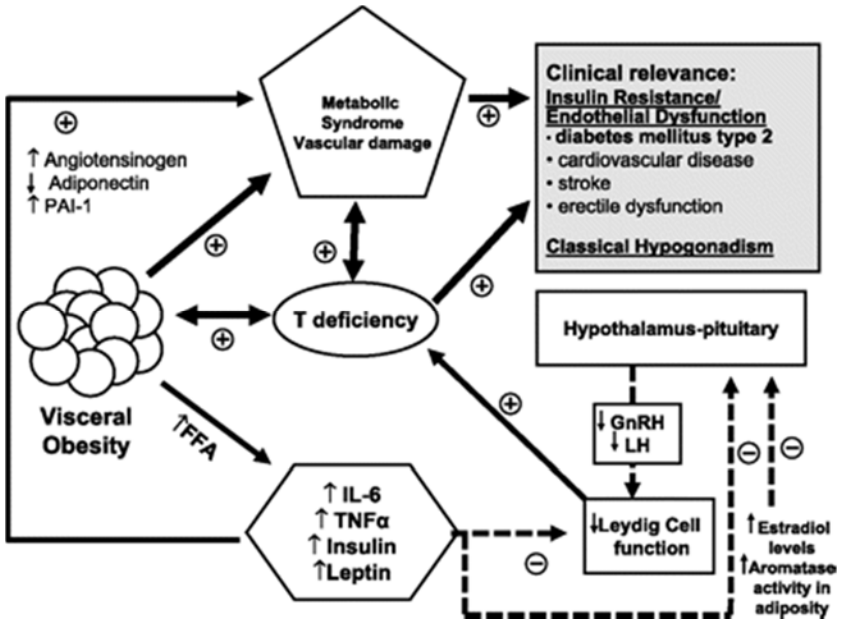
The proposed mechanism of how obesity and inflammation promotes insulin resistance is through the release of excess of FFA. This in turn through the nuclear factor-κB pathways produces augmented synthesis of TNF-α, interleukin 6 and MCP-1. The former factor causes increased lipolysis and formation of excess of free fatty acid while the latter factors cause more and more recruitment of other inflammatory cells and all these alters the sensitivity

of insulin. Other mechanism of actions of these inflammatory mediators is an increased expression of the adhesion molecules in the endothelium of the blood vessels and also in its smooth muscles mediated by TNF-α. Apart from this TNF-α also causes a dysregulation between the vasoconstriction mediated by ET-1 and the vaso relaxtion induced by nitric oxide ultimately favouring vasoconstriction; similarly CRP, though nonspecific, a marker of inflammation IL-6 is increased through IL-6 mediated enhanced hepatic synthesis. Adipokines, [127] another important mediator modulates chemotaxis and adhesion of inflammatory cells especially monocytes and facilitates its conversion in to macrophages.

Normally the conversion of testosterone to estrogen [83] occurs in the adipocytes because the enzyme aromatase is located in the fat cells. In the presence of obesity the amount of fat tissue mass that can act as a site for this conversion increases and hence there is more aromatisation reaction taking place thereby decreasing the serum level of testosterone due to its excessive conversion in to estrogen in the adipocytes. This in turn activates the hypothalamic E2 receptors and produces feedback inhibition of the gonads. Thus aromatase inhibitors play a role in attenuating the symptoms of hypogonadism in obese men [128].

Testosterone and atherogenesis:

Testosterone has an antithrombotic effect on the clotting mechanism. There is an inverse relationship between the prothrombotic clotting factors, fibrinogen and the tissue plasminogen activator inhibitor 1. It also has a direct relationship with the plasminogen activator activity [129]. Thus the presence of normal levels of testosterone concentrations is necessary for maintaining proper blood homeostasis.



From experimental studies it has become evident that testosterone slows down the atherogenesis [130]. Iatrogenic orchidectomy in mouse led to the development of atherosclerotic plaques in the aorta. Another important point to be noted is that, irrespective of the lipid profile, testosterone slows down the progress of atherosclerosis. Testosterone replacement therapy has thus retarted

atherogenesis [131] and the further development of cardiovascular risk. By inhibition of the inflammatory mediators testosterone reverses prothrombotic environment. Testosterone reduces the early progression of atherosclerosis by a major mechanism by which it gets converted to estradiol in the walls of the blood vessel by the reaction of aromatization. This can be proved by the increase in the progression of atherosclerosis in patients on aromatase inhibitors.

Testosterone Levels and Cardiovascular Disease (CVD)

It was initially presumed that high levels of testosterone produce adverse effects on the heart and the vascular system. But latter there was a consensus that high normal range of testosterone level did not produce any risk to the cardiovascular system. Presently it has been found through many meta-analyses that lower levels of testosterone are associated with a stronger positive correlation to the development of adverse cardiovascular effects. The most important effects by which hypotestosteronemia can induce atherosclerosis and hence coronary artery disease includes alteration of hemostatic mechanics towards a prothrombotic as well as a fibrinolytic state, increased insulin resistance along with an adverse lipid profile [132]. It has also been proven by experimental studies that castration of the testes resulted in increased risk of atherosclerosis whereas testosterone administration diminished the risk.

Apart from decreasing the adverse cardiac effects testosterone also has many beneficial effects on the heart. Testosterone has a strong vaso-relaxing effect on the coronary vasculature [133]. This effect is caused by testosterone induced calcium channel blockade in the smooth muscles of the blood vessels. This action of testosterone has been used to raise the threshold of angina in men with hypotestosteronemia thereby decreasing the development of angina [134]. Testosterone is also beneficial in the treatment of chronic congestive heart failure by increasing the functional capacity and by improving the insulin sensitivity. [135]

With the knowledge of the available studies it can be thus concluded that for optimal cardiovascular health it is always necessary to maintain the level of plasma testosterone about the mid-range of the normal values. It has also been shown that testosterone levels both below or above the normal values pertaining the particular age has found to raise the cardiovascular risks especially [136]. Thus is the need for maintaining a normal testosterone level to prevent increased cardiovascular mortality.

In summary, hypotestosteronemia has a definitive risk on the cardiovascular wellbeing. By producing adverse effects on various metabolic parameters they increase the risk and create a pro inflammatory, prothrombotic state promoting atherogenesis. All these effects can be reversed by testosterone replacement therapy. The coronary vasodilatory effect has been claimed for the

improvement that it produces in angina thereby reducing myocardial ischemia [137]. Recent studies have shown that the use of testosterone administration in the improvement of chronic heart failure [138]. Thus it has been found by recent studies that the mortality rates in men from cardiovascular death are much more in men with hypotestosteronemia rather than men with a normal range of serum testosterone level.

TESTOSTERONE REPLACEMENT THERAPY:

The aim of testosterone replacement therapy is to produces symptomatic relief in patients with hypogonadism. This is achieved by bringing the testosterone levels to near normal with the help of exogenous synthetic hormones. With the emergence of novel methods for the delivery of testosterone these have become possible [139]. Some of the newer modes of testosterone delivery include 1% testosterone gel, transdermal testosterone patch, buccal, bioadhesive, T tablets, testosterone pellets, testosterone-inadhesive matrix patch [140] and depot intramuscular injections. Further moving one step ahead, testosterone replacement in patients with type 2 diabetes mellitus who suffer from hypotestosteronemia, there is multiplicity of benefits. Apart from relief of symptoms pertaining to hypogonadism and stabilization of glycemic control, it also has a positive effect on the following: reduction of blood pressure, normalization of the lipid profile with reduction in the obesity and other metabolic parameters [141]. Further perspective is that either in normal or in

diabetic men, testosterone increases the insulin sensitivity in patients with hypogonadism. Furthermore studies have proved that there is a marked reduction in the insulin resistance in diabetic men with hypotestosteronism [142]. Similarly in patients with chronic congestive cardiac failure, it has been found that insulin resistance is a common entity. Thus administration of testosterone in such patients has decreased the insulin resistance. Thus it is evident that testosterone improves the insulin sensitivity, irrespective of whether an individual has glucose intolerance or not.

The important mediators involved in producing insulin resistance are proposed to be the inflammatory cytokines i.e. interleukins 1 beta and 6, tumor necrotic factor alpha etc. Testosterone has been found to decrease the synthesis of these inflammatory mediators, thereby improving the insulin sensitivity. And also organs involved in insulin resistance like the liver, adipose tissue and muscles are affected by testosterone. By these mechanisms testosterone produces a decline in insulin resistance.

Another important aspect of testosterone treatment is that it decreases body fat and thereby the body mass index and waist and hip circumference in men with hypogonadism, irrespective of whether they are obese or not [143]. These parameter are one of the important markers for the development of metabolic syndrome or syndrome X, which in turn is the main risk factor for the development of atherosclerotic diseases, especially coronary artery disease and

stroke. Similarly central obesity which is considered one of the markers for the metabolic syndrome has been found to decrease after testosterone replacement. Another factor, the Leptin is related to body fat amount. In patients with metabolic syndrome and hypogonadism treatment with testosterone has shown to decrease the leptin levels [144].

Testosterone also affects the lipid profile positively. This has been proved by many studies undertaken in patients with metabolic syndrome. These studies have shown that testosterone replacement have shown to produce a considerable fall in the total cholesterol levels. It also produces a small though significant fall in the LDL cholesterol [145]. But the effect of testosterone on the HDL cholesterol is not predictable; it may show an increase, decrease or may even remain unchanged. Some studies have also shown that after an initial reduction in HDL cholesterol, it rises back to its previous values. The triglyceride levels remain unchanged with testosterone therapy. Another important lipid fraction which has been presently given more importance due to its strong positive relation with coronary heart disease [146] is Lipoprotein a, Lp(a). It is associated with especially premature coronary artery disease than the other lipid fractions. It has been found that, in patients with hypotestosteronemia with syndrome X or with diabetes mellitus this testosterone replacement therapy has found to produce a significant reduction in Lipoprotein a, Lp (a) level, thereby reducing the cardiovascular risks.

Another important aspect is that there are a number of studies done on the testosterone replacement therapy, but it has not proved by any of the studies that testosterone administration has produced any adverse cardiovascular accidents, cardiac risks or has produced increased mortality. All these are favorable for the future developments in this field of treatment.

To summarize testosterone replacement has produced a significant decline in the cardiovascular risk factors [147], such as improving insulin sensitivity, stabilizing the glycemic levels, maintaining normal blood pressure, reducing central obesity, normalizing the lipid profile and reducing the inflammatory state in which the body ensues apart from maintaining the sexual functions.

Testosterone in Diabetic foot:

Sensory motor neuropathy, foot ulcers, peripheral vascular disease and infections are the most common cause of lower limb complications in diabetes mellitus [148]. Infections in the foot are the commonest cause of limb amputation in diabetic patients. Ulcerations in the foot are mainly due to 1) Peripheral vascular disease 2) Sensory neuropathy 3) Repeated minor trauma to the foot 4) Arch abnormalities. These complications of the foot improve well with testosterone administration.

These beneficial effects may be due to:

1) Testosterone increases the haemoglobin concentration by stimulating erythropoiesis.

2) Studies have shown that there is a relation between testosterone levels and peripheral vascular disease [149]. This is mainly due to the action of testosterone on the vascular smooth muscles. Testosterone causes vasodilatation mainly through smooth muscle relaxation, which does not require the endothelium, although an endothelium may contribute as shown by few studies [150]. Although the precise mechanism that causes this vasodilatory effect is still on debate, the proposed mechanism is either due to the activation of K (+) channels or due to the of Ca (2+) channels blockage in the myocytes of the blood vessels[151].

Knowledge of this action of testosterone paves way for the utilisation of testosterone replacement therapy [152] in the healing of diabetic foot ulcers. Testosterone administration improves the vascular integrity and functions. Along with its vasodilatory effect testosterone improves the local oxygen pressure in the blood vessels thereby improving the vascular functions and promoting the healing of ulcers.

3) The anabolic action of testosterone through its protein synthesizing capacity also is responsible for its beneficial effect in addition to its effects on the vasculature [153].

4) Testosterone also has effect on the platelets and clotting mechanism. In experimental studies androgens are found to inhibit the aggregation of platelets mainly induced by oxidative stresses. This is due to the decreased release of thromboxane A (2) from the platelets [154]. Testosterone also affects the fibrinolytic pathway positively. As a result of these mechanism the blood flow to the foot microvasculature increases thereby promoting wound healing.

5) The present model for the origin and progression of atherosclerosis and hence cardiovascular diseases is the response-to-injury hypothesis. According to this hypothesis atherosclerosis is a chronic inflammatory response of the arterial wall to endothelial injury. Inflammation is therefore a key factor in the development of coronary heart diseases [155]. Treatment with testosterone has found to show a decrease in the inflammatory mediators which are involved in this process. In doing so it regulates the integrity and function of the endothelium. [156].

MATERIALS AND METHODS

STUDY DESIGN

- Case control study

STUDY CENTRE

- Government General Hospital, Chengalpattu

SELECTION OF PATIENTS

1. INCLUSION CRITERIA

1. Men with type 2 Diabetes Mellitus between the age of 35-75yrs

2. Men with no H/O Diabetes Mellitus with FBS < 126 mg/dl between the age of 35-75yrs

2. EXCLUSION CRITERIA:

1. Patients with Chronic Liver Disease

2. Patients with chronic infections like HIV, TB

3. Patient on anabolic steroids

4. Patients on Chemotherapy or Radiotherapy

5. Patients with Primary Hypogonadism

3. SAMPLE SIZE

- 100 patients with Type 2 Diabetes Mellitus between the age of 35-75yrs
- 100 non diabetic men of the same age group

MATERIALS AND METHODS

METHODOLOGY:

We started the study with the selection of cases and controls. We selected 100 diabetic men from our Diabetology OPD, Chengalpattu Medical College who fitted in to the inclusion criteria as our cases. As controls we selected subjects without history of diabetes mellitus whose FBS was less than 126 mg/dl on two occasions, from our male Medical OP. Informed consent was obtained from all subjects. A detailed history regarding the duration of diabetes, the patients other associated risk factors like hypertension, coronary artery disease was obtained. Anthropometric measurements like height, weight, waist and hip circumferences were measured. BMI was calculated by obtaining the ratio of the weight and the square of height (kg/m^2). Waist-Hip ratio was also calculated. Fasting blood sugar and postprandial blood sugar were measured using chromatography method. Total cholesterol was also measured. Total testosterone in the early morning (8:00–10:00 AM) was measured using CLIA (Chemiluminescence enzyme immunoassay) method. The normal range for early morning total testosterone in adult males is considered between 300ng/dl and 900ng/dl.

The average serum testosterone levels were compared between the diabetic and non-diabetic men and was statistically analysed. The diabetic patients were further grouped based on the duration of diabetes, BMI,

cholesterol levels and presence or absence of associated risk factor and analysed.

STATISTICAL ANALYSIS:

The T-test for independent samples was used.

DATA COLLECTION AND ANALYSIS

Collection of data: As per Performa attached.

Analysis of data: Using statistical package SPSS software

Conflict of interest: NIL

Financial support: NIL

OBSERVATIONS AND RESULTS

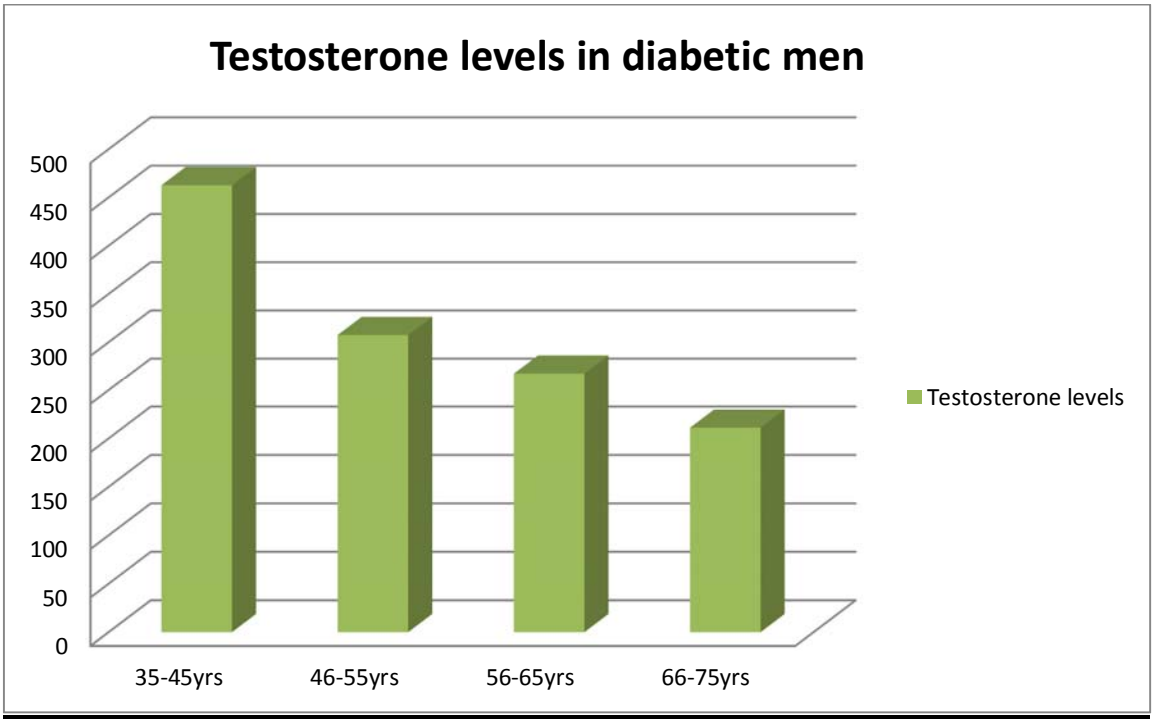
We conducted the study from April 2012 to September 2012 and we analyzed 100 diabetic and 100 non diabetic men from whom samples were collected for the estimation of serum levels of total testosterone.

Among the diabetic men, the average testosterone values were calculated and grouped according to the age categories.

Table 1: Testosterone levels according to age group in diabetic men

S.No	Age (yrs.)	No of subjects	Avg Serum Testosterone (ng/dl)
1.	35-45	15	462.73
2.	46-55	51	307.51
3.	56-65	27	267.41
4.	66-75	07	211.14

Figure 1: **Testosterone levels according to age group in diabetic men**

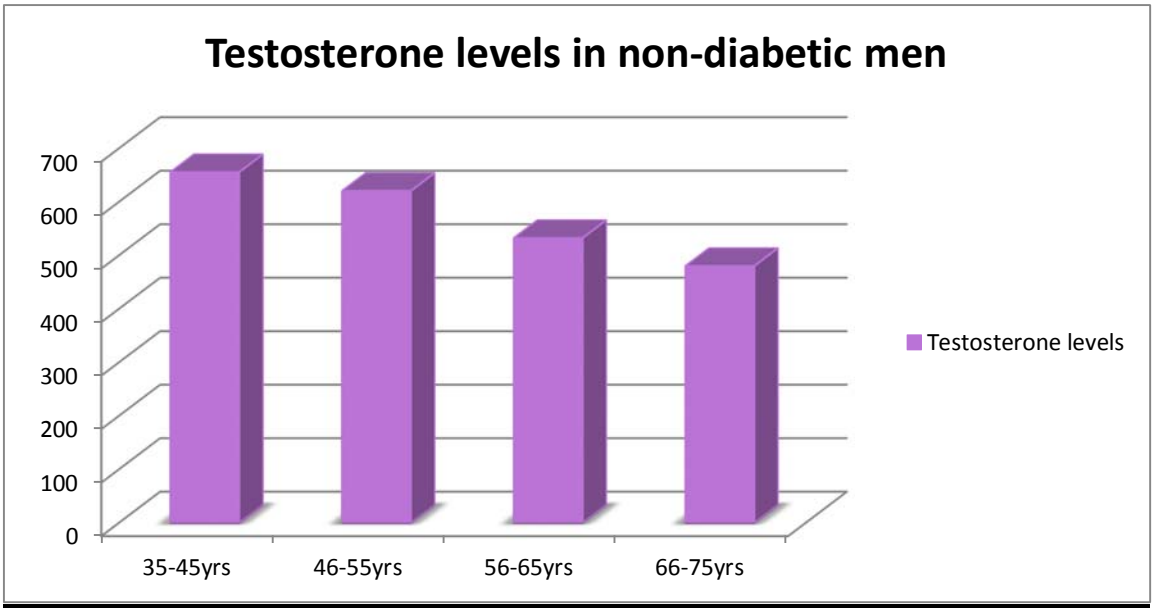


Similarly average testosterone was calculated for the non-diabetic men and grouped.

Table 2: Testosterone levels according to age group in non-diabetic men

S.No	Age (yrs)	No of subjects	Avg Serum Testosterone (ng/dl)
1.	35-45	15	655.53
2.	46-55	50	620.46
3.	56-65	25	532.30
4.	66-75	10	480.00

Figure 2: Testosterone levels according to age group in non-diabetic men

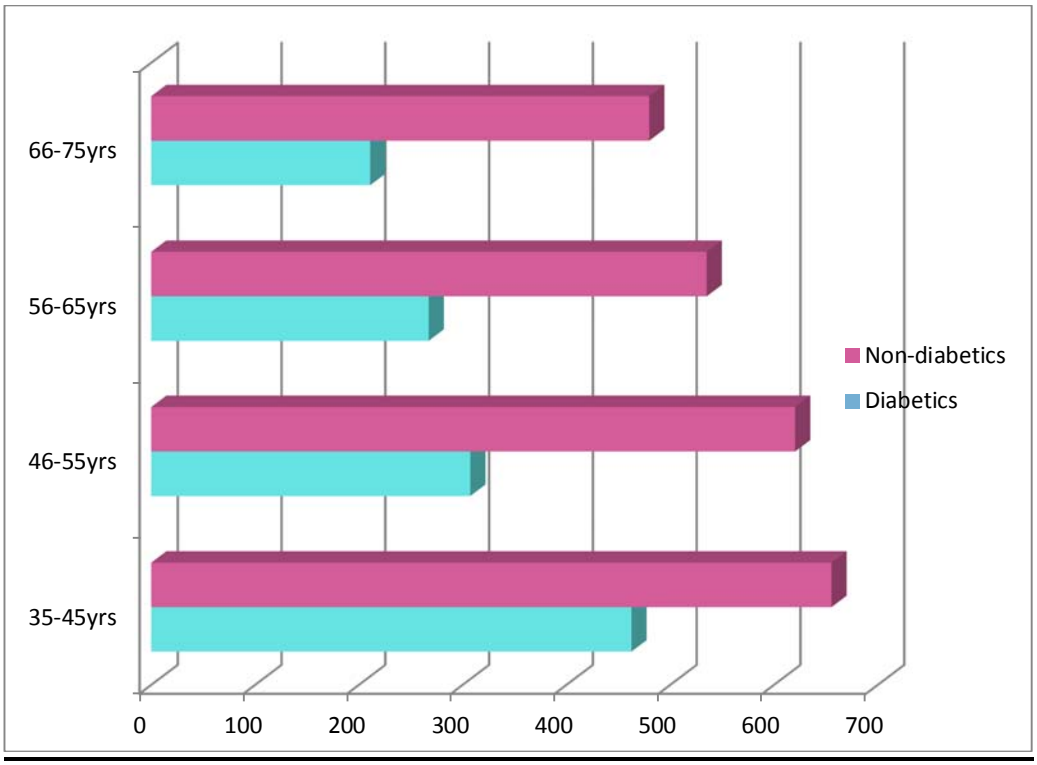


On comparing the testosterone level we found that, there was a significant decrease in the testosterone levels between the diabetics and non-diabetics in each age group.

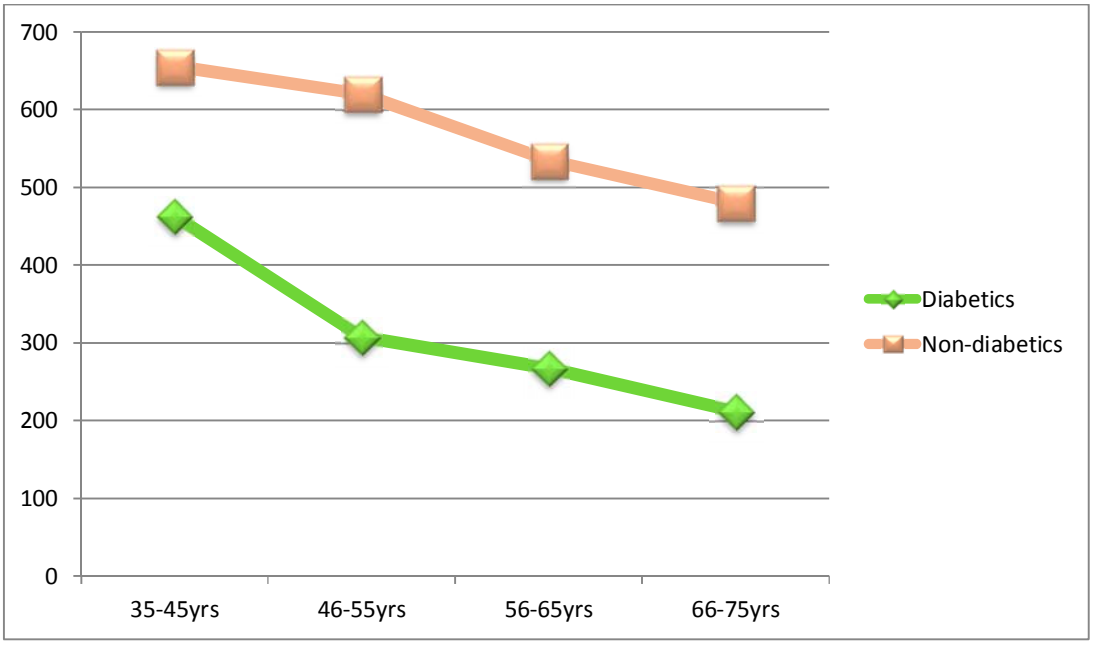
Table 3: Comparison of the total testosterone levels between diabetics and non-diabetics

S.No	Group	35-45yrs	46-55yrs	56-65yrs	66-75yrs
1.	Diabetic men	462.73	307.51	267.41	211.14
2.	Non-diabetic men	655.53	620.46	532.30	480.00

<u>Figure 3:</u> Comparison of the testosterone levels between diabetics and non-diabetics



<u>Figure 4:</u> Comparison of the testosterone levels between diabetics and non- diabetic



Statistical analysis was done with the student T test for independent samples. P values where calculated for each age group.

Table 4: P values for different age groups

S.NO	Age group (yrs)	Diabetics TT (ng/dl)	Non-Diabetics TT (ng/dl)	P value
1.	35-45	462.73	655.53	0.028
2.	46-55	307.51	620.46	0.01
3.	56-65	267.41	532.30	0.001
4.	66-75	211.14	480.00	0.001

SPSS Output

35-45yrs:

T-Test

Group Statistics

Code		N	Mean	Std. Deviation	Std. Error Mean
Stlevel	Diabetic	15	462.73	125.238	32.336
	Non Diabetic	15	655.53	136.471	35.237

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
		Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
Stlevel	Equal variances assumed	1.631	.212	-7.723	28	**.028**	-369.333	47.825	-467.299	-271.368
	Equal variances not assumed			-7.723	27.796	.028	-369.333	47.825	-467.331	-271.335

46-55yrs:

T-Test

Group Statistics

Code1		N	Mean	Std. Deviation	Std. Error Mean
Stlevel1	Diabetic	51	307.51	108.389	15.177
	Non Diabetic	50	620.46	91.755	12.976

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
		Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
Stlevel1	Equal variances assumed	2.061	.154	-16.646	99	**.001**	-332.950	20.001	-372.637	-293.263
	Equal variances not assumed			-16.674	96.952	.001	-332.950	19.968	-372.582	-293.318

56-65yrs:

T-Test

Group Statistics

	Code2	N	Mean	Std. Deviation	Std. Error Mean
Stlevel2	Diabetic	27	267.41	93.777	18.047
	Non Diabetic	25	532.30	170.914	34.183

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
		Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
Stlevel2	Equal variances assumed	.687	.411	-6.999	50	**.0001**	-264.893	37.848	-340.912	-188.873
	Equal variances not assumed			-6.853	36.618	.0001	-264.893	38.655	-343.242	-186.543

66-75yrs:

T-Test

Group Statistics

	Code3	N	Mean	Std. Deviation	Std. Error Mean
Stlevel3	Diabetic	7	211.14	66.261	25.044
	Non Diabetic	10	480.00	168.419	53.259

Independent Samples Test

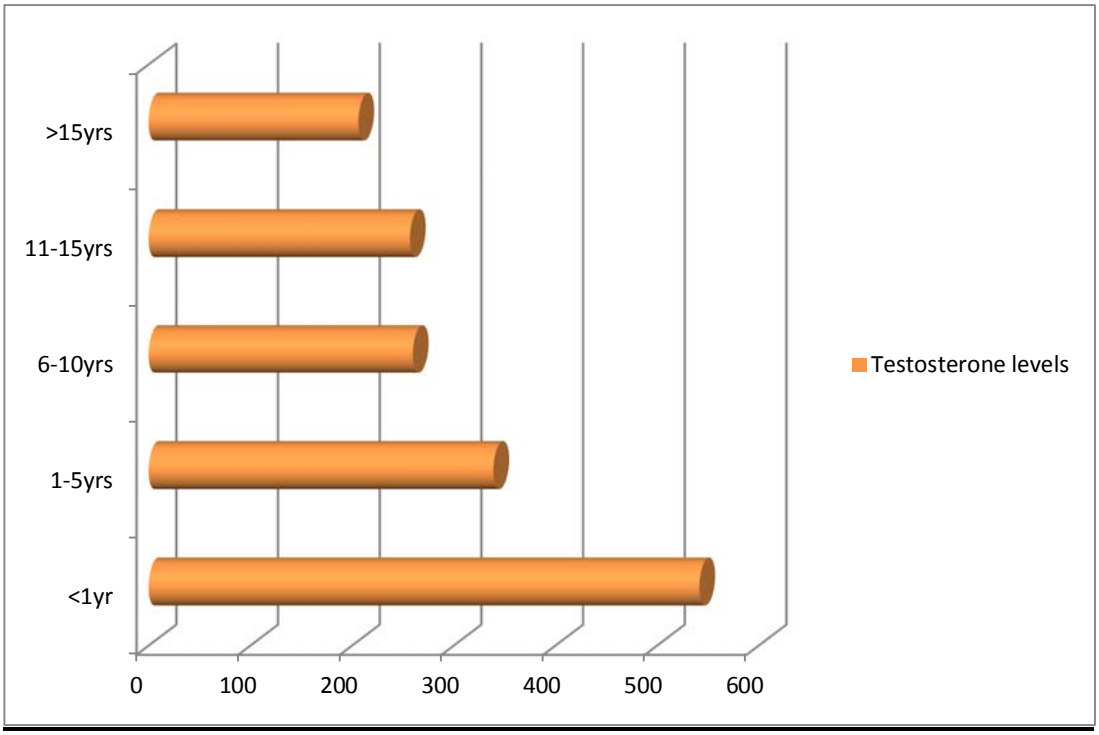
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
		Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
Stlevel3	Equal variances assumed	5.724	.030	-5.462	15	**.001**	-368.857	67.526	-512.785	-224.930
	Equal variances not assumed			-6.267	12.503	.001	-368.857	58.853	-496.518	-241.197

We analyzed the other associated factors in the diabetic men. We grouped the duration of diabetes and analyzed the testosterone levels and compared them.

Table 5: Testosterone levels according to the duration of diabetes

S.No	Duration of Diabetes	No of subjects	Avg Serum Testosterone (ng/dl)
1.	<1yr	8	541.62
2.	1-5yrs	49	339.06
3.	6-10yrs	20	259.85
4.	11-15yrs	11	257.01
5.	>15yrs	12	206.33

Figure 5: Testosterone levels according to the duration of diabetes

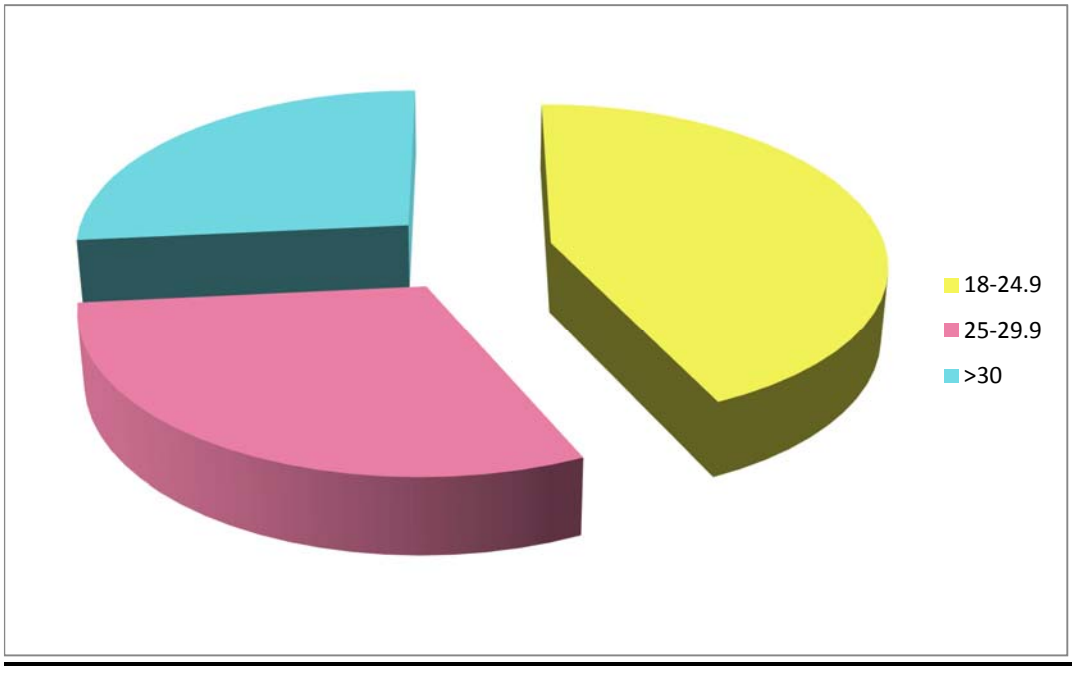


Body mass index was calculated by obtaining the ratio of the weight and the square of height (kg/m²). The testosterone levels were then compared between the different BMI.

Table 6: Testosterone levels according to the Body Mass Index

S.No	BMI	No of subjects	Avg Serum Testosterone (ng/dl)
1.	18-24.9	57	368.70
2.	25-29.9	29	258.51
3.	>30	14	226.64

Figure 6: Testosterone levels according to the Body Mass Index

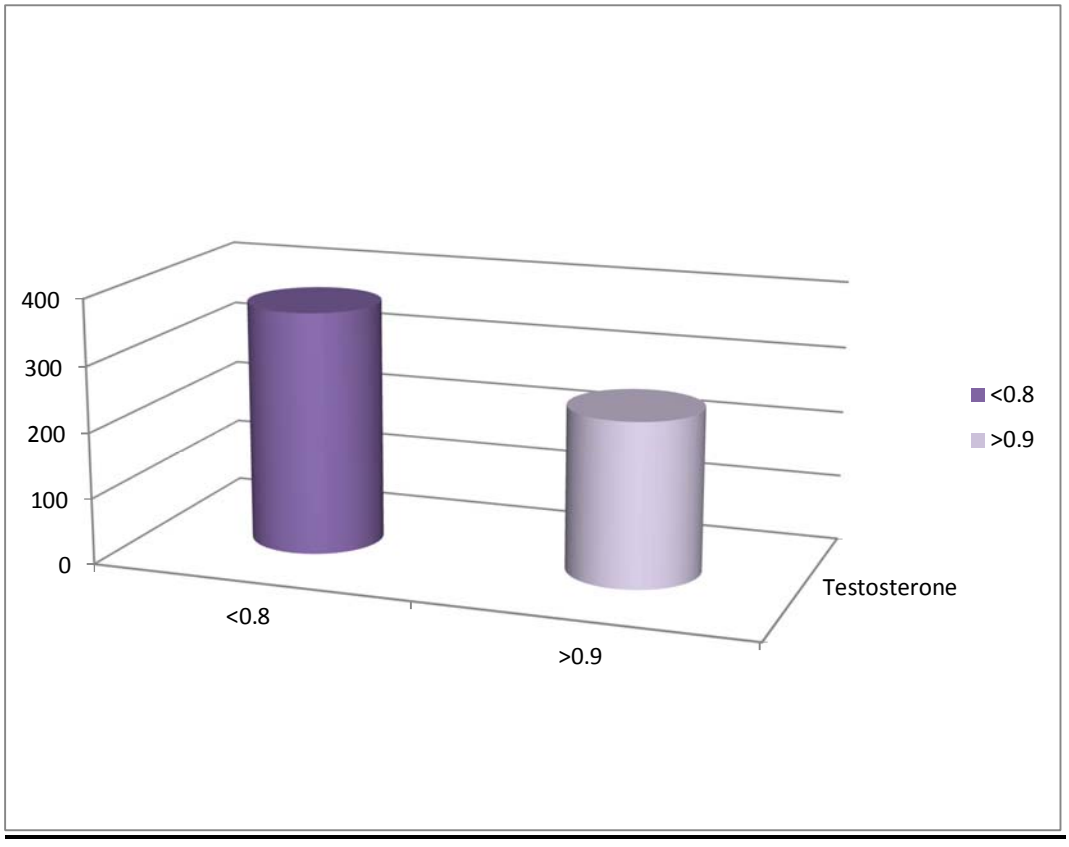


Also the waist - hip ratio was calculated and the testosterone levels were compared.

Table 7: Testosterone levels according to the Waist-Hip ratio

S.No	W/H ratio	No of subjects	Avg Serum Testosterone (ng/dl)
1.	<0.8	57	368.71
2.	>0.9	43	248.14

Figure 7: Testosterone levels according to the Waist-Hip ratio

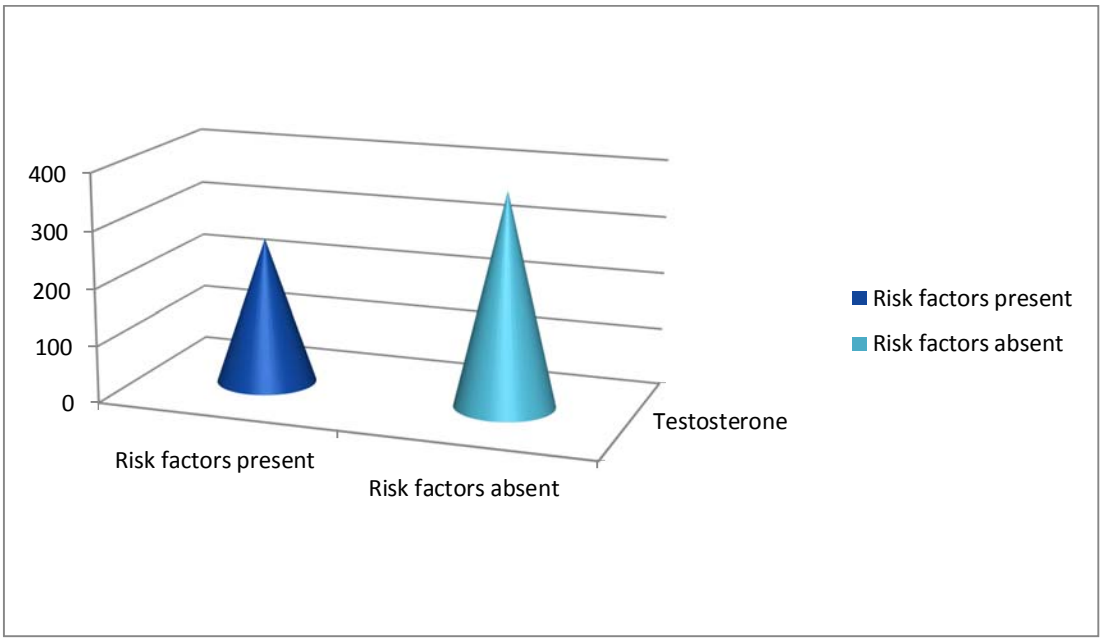


There other risk factors such as hypertension, cardiovascular diseases were also analyzed. Those diabetic men with these risk factors were separated into one group and those without as other group and their testosterone levels were compared.

Tables 8: Testosterone levels according to the presence or absence of other risk factors.

S.No	Associated Risk factors	No of subjects	Avg Serum Testosterone (ng/dl)
1.	Present	51	257.17
2.	Absent	49	374.18

Figure 8: Testosterone levels according to the presence or absence of other risk factors.

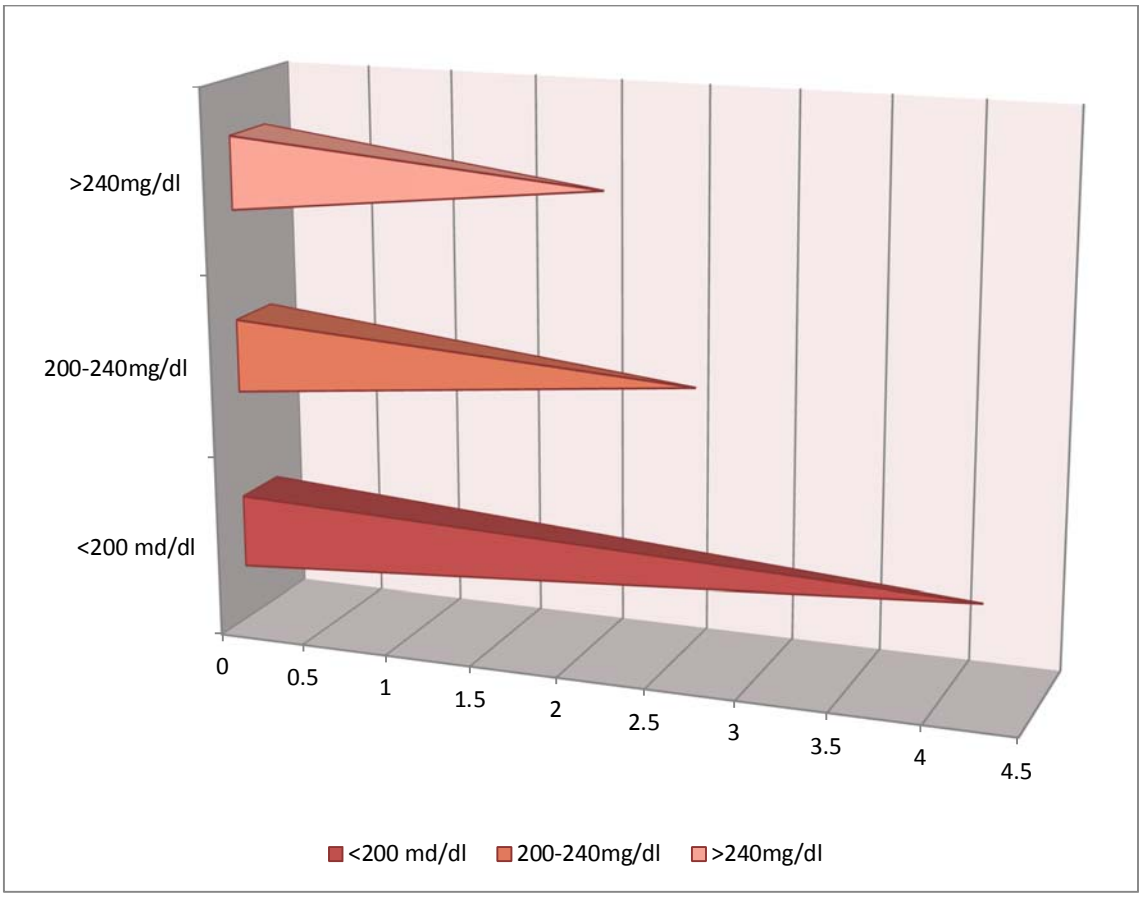


The testosterone levels were then compared according to the cholesterol levels in the diabetic men and were separated in to different group, according to the cholesterol levels as < 200 mg/dl to be normal, 200-240mg/dl as moderate risk and >240 mg/dl as high.

Table 9: Testosterone levels according to the serum Cholesterol

S.No	Serum Cholesterol (mg/dl)	No of subjects	Avg Serum Testosterone (ng/dl)
1.	<200	38	4.184
2.	200-240	47	2.604
3.	>240	15	2.082

<u>Figure 9:</u> Testosterone levels according to the serum Cholesterol



DISCUSSION

Diabetes Mellitus which was once considered as a disease of minor significance has now become one of the major epidemic and a global health problem. It is one of the most common non- communicable diseases globally, with around 290 million people suffering from diabetes worldwide. The proportion of diabetes in India is steadily on a rise and in another fifteen years India would have the largest number of diabetics in the world. It has been well known about the most dreaded micro-vascular and macro-vascular complications of diabetes mellitus but the other endocrinological perspectives of diabetes are often not given importance.

Our study was conducted in Chengalpattu Government Medical College Diabetology OPD which caters around 300 patients per day as outpatients. 100 diabetic men and 100 non diabetic men were selected and serum total testosterone assay was done. Average testosterone values were calculated for different age groups. The results were then compared age-wise and the patterns of testosterone in each age group were analyzed in diabetic and non-diabetic men. The average testosterone values between the diabetic and non-diabetic men in the age group of 35-45yrs was 462.73ng/dl and 655.53ng/dl respectively, in the age group of 46-55yrs was 307.51ng/dl and 620.46ng/dl respectively, in the age of 56-65yrs was 267.41ng/dl and 532.3ng/dl

respectively, in the age group 66-75yrs was 211.14ng/dl and 480ng/dl respectively.

Statistical analysis was made and the P values were calculated by the student T- test. The association between the diabetic and non-diabetic in each age group was found to be significant with a P-value of <0.05. Thus the decrease in the serum level of testosterone is found to be significant. We also found that as the age progresses, there is a steady decline in the serum levels of testosterone in both the groups. But the fall in the testosterone values is much more significant in the diabetics.

We did the second part of the study, where we divided the diabetic men into smaller sub groups and compared different parameters. Firstly according to the duration of diabetes we grouped the patients. We found in our study that, as the duration of diabetes increases the fall in the serum testosterone level became more significant with around normal values up to 5yrs of diabetes and later declining.

The next parameter we evaluated was the Body mass index and Waist hip ratio. In both the groups we found that as the BMI and the W/H ratio increases there is a decrease in the serum levels of testosterone, thereby suggesting an inverse relation between these parameters and testosterone levels.

The other parameters we evaluated were, to compare the effects of other risk factors. Out of these, we considered risk factors like hypertension or coronary artery disease and grouped them into those with risk factors and those without. We compared the testosterone values between these two groups and found that, there was a decline in the serum testosterone values in patients with associated other risk factors than those without risk factors.

Finally we segregated the diabetic patient with different levels of serum cholesterol and separated them in to three groups and found that this relation to be inverse, that is as the serum cholesterol levels increases the serum testosterone level decreases with a normal level of 4.1mg/dl when the cholesterol is <200mg/dl and values of around 2.08mg/dl when cholesterol is >250mg/dl.

Thus we also evaluated the effects of multiple risk factors on diabetic men and testosterone levels.

CONCLUSION

Thus we conclude that there is a significant reduction in the levels of serum testosterone in diabetic men as compared to that of non-diabetic men. Even though the declining trend of the testosterone levels occurs as the age increases, the reduction in the testosterone levels are more significant in the diabetic group as compared to that of the non-diabetic men. Thus from our study, we propose that age factor alone is not the cause of hypotestosteronemia in diabetic men.

From the analyses of different factors like BMI, cholesterol and other risk factors we have shown the influence of multiple factors on the levels of testosterone, in which most of them has an inverse correlation.

Thus, in diabetic patients, hypotestosteronemia is a common entity. Though the symptoms of low testosterone are non-specific, a detailed symptomatic analysis would pave way to bring to light this hidden epidemic. Hence we suggest the measurement of testosterone in patients with diabetes, as the replacement of testosterone can have multiple benefits in diabetic patient to prevent diabetic complication and cardiovascular diseases.

Testosterone level can further predict the development of type 2 diabetes mellitus, the utilization of this aspect of testosterone in future, is not too far.

LIMITATIONS

This study has the following limitations:

1. The level of sex hormone binding globulin, which is a confounding factor, was not calculated.
2. The level of free testosterone was not computed.
3. The actual duration of diabetes may not be accurate.

ABBREVIATIONS

T	Testosterone
FT	Free Testosterone
TT	Total Testosterone
DHT	Dihydrotestosterone
DHEA	Dehydroepiandrsterone
SHBG	Sex hormone–binding globulin
GnRH	Gonadotrophin releasing hormone
FSH	Follicle stimulating hormone
LH	Luteinizing hormone
AR	Androgen receptor
T2DM	Type 2 diabetes mellitus
CRP	C reactive protein
BMI	Body mass index
W/H	Waist hip ratio
kDa	Kilo dalton
DNA	Deoxy ribonucleic acid

RNA	Ribonucleic acid
RNAP	Ribonucleic acid polymerase
BMD	Bone mineral density
ED	Erectile dysfunction
LC-MS	Liquid chromatography tandem mass spectrometry
HPLC	High-performance liquid chromatography
MS	Mass spectrometry
hCG	Human chorionic gonadotropin
MIS	Mullerian inhibiting substance
CVD	Cardiovascular disesase
Lp(a)	Lipoprotein A
TNF	Tumor necrotic factor
IL	Interleukins
PCG	Peroxisome proliferator–activated receptor-γ coactivator
OXPHOS	Oxidative phosphorylation
OLETF	Otsuka Long Evans Fatty
FFA	Free fatty acid

PROFORMA

Name :

Age :

Sex :

Occupation :

Marital status :

Address :

IP. No :

BRIEF PATIENT HISTORY:

Duration of Diabetes :

H/o any Chemotherapy or Radiation :

H/o any chronic medical illness :

High risk behavior :

	DURATION	MEDICATIONS
DIABETES MELLITUS		
SYSTEMIC HYPERTENSION		
CORONARY ARTERY DISEASE		

HABITS	DURATION	QUANTITY
Smoking		
Alcoholism		

FAMILY H/O	Father	Mother	Siblings
DIABETES MELLITUS			
SYSTEMIC HYPERTENSION			
CORONARY ARTERY DISEASE			

PHYSICAL EXAMINATION

MEASUREMENTS:

Height :

Weight :

Waist circumference :

Hip circumference :

BODY MASS INDEX :

WAIST HIP RATIO :

GENERAL EXAMINATION

VITAL SIGNS

Pulse Rate :

Blood Pressure :

Respiratory rate :

Temperature :

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM :

GASTROINTESTINAL SYSTEM :

CENTRAL NERVOUS SYSTEM :

INVESTIGATIONS

CBC

TC

DC

HB

HEMATOCRIT

ESR

PLATELETS

LFT

TOTAL BILIRUBIN

AST

ALT

SAP

TOTAL PROTEIN

RFT

BLOOD SUGAR- **FBS**

PPBS

UREA

SERUM CREATININE

Na+

K+

FASTING LIPID PROFILE

SERUM TESTOSTERONE

HIV :

USG ABDOMEN :

BIBLIOGRAPHY:

1. David KG., Dingemanse E, Freud J. Laqueur E (May 1935). "Über krystallinisches mannliches Hormon aus Hoden (Testosteron) wirksamer als aus harn oder aus Cholesterin bereitetes Androsteron [On crystalline male hormone from testicles (testosterone) effective as from urine or from cholesterol]" (in German). Hoppe Seylers Z Physiol Chem 233 (5–6): 281. doi:10.1515/bchm2.1935.233.5-6.281

2.http://www.oocities.org/westhollywood/park/3638/hormones 3. Freeman ER, Bloom DA, McGuire EJ (February 2001). "A brief history of testosterone". J. Urol. 165 (2): 3713. doi:10.1097/00005392-200102000-00004.

4. Marc, Klein (1970–80). "Berthold, Arnold Adolphe". Dictionary of Scientific Biography. 2. New York: Charles Scribner's Sons. pp. 72-73. ISBN 0684101149.

5. Berthold, A.A., 1849. Transplantation der Hoden. Arch. Anat. Physiol. Wissenschr. Med. pp. 42-46.

6. Mehta, P. H., & Josephs, R. A. (in press). Testosterone. In R.Baumeister & K. D. Vohs (Eds.), Encyclopedia of Social Psychology. Thousand Oaks, CA: Sage.

7. Ruzicka L, Wettstein A (1935). "Uber die kristallinische Herstellung des Testikelhormons, Testosteron (Androsten-3-ol-17-ol) [The crystalline production of the testicle hormone, testosterone (Androsten-3-ol-17-ol]" (in German). Helvetica Chimica Acta 18: 1264–1275. doi:10.1002/hlca.193501801176

8. Reed WL, Clark ME, Parker PG, Raouf SA, Arguedas N, Monk DS, Snajdr E, Nolan V, Ketterson ED (May 2006). "Physiological effects on demography: a long-term experimental study of testosterone's effects on fitness". Am. Nat. 167 (5): 667–83. doi:10.1086/50305

9. Haddad RM, Kennedy CC, Caples SM, Tracz MJ, Boloña ER, Sideras K, Uraga MV, Erwin PJ, Montori VM (January 2007). "Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials". Mayo Clin. Proc. 82 (1): 29–39. doi:10.4065/82.1.29. PMID 17285783

10. Mooradian AD, Morley JE, Korenman SG (February 1987). "Biological actions of androgens". Endocr. Rev. 8 (1): 1–28. doi:10.1210/edrv-8-1-1

11. Butenandt A, Hanisch G (1935). "Uber die Umwandlung des Dehydroandrosterons in Androstenol-(17)-one-(3) (Testosterone); um Weg zur Darstellung des Testosterons auf Cholesterin (Vorlauf Mitteilung). [The conversion of dehydroandrosterone into androstenol-(17)-one-3 (testosterone); a

method for the production of testosterone from cholesterol (preliminary communication)]" (in German). Chemische Berichte 68: 1859–1862.

12. Ruzicka L, Wettstein A (1935). "Uber die kristallinische Herstellung des Testikelhormons, Testosteron (Androsten-3-ol-17-ol) [The crystalline production of the testicle hormone, testosterone (Androsten-3-ol-17-ol]" (in German). Helvetica Chimica Acta 18: 1264–1275. doi:10.1002/hlca.193501801176.

13. "Testosterone Information". http : // www. drugs. com / testosterone . html.

14."Striant Official FDA information, side effects and uses". http://www.drugs.com/pro/striant.html.

15."AndroGel Official FDA information, side effects and uses". http://www.drugs.com/pro/androgel.html.

16."Testim (patches and gel) medical facts". http://www.drugs.com/mtm/testim-patches-and-gel.html.

17."Testopel Pellets". www.slatepharma.com.

18. Hoberman JM, Yesalis CE (February 1995). "The history of synthetic testosterone". Sci. Am. 272 (2): 76–81. doi:10.1038/scientificamerican0295-76

19. Karges, W.; Schaaf, L.; Dralle, H.; Boehm, B. O. (2000). "Concepts for screening and diagnostic follow-up in multiple endocrine neoplasia type 1

(MEN1)*". Experimental and Clinical Endocrinology & Diabetes 108 (5): 334–340. doi:10.1055/s-2000-8146

20. Haddad RM, Kennedy CC, Caples SM, et al. Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials. Mayo Clin Proc 2007;82:29e39.

21. Jones RD, Nettleship JE, Kapoor D, et al. Testosterone and atherosclerosis in aging men: purported association and clinical implications. Am J Cardiovasc Drugs 2005;5:141e54.

22. Simon D, Charles MA, Nahoul K, Orssaud G, Kremski J, Hully V, Joubert E, Papoz L, Eschwege E. Association between plasma total testosterone and cardiovascular risk factors in healthy adult men: The Telecom Study. J Clin Endocrinol Metab. 1997;82:682-685.

23. Kapoor D, Goodwin E, Channer KS, et al. Testosterone replacement therapy improves insulin resistance, glycaemic control, visceral adiposity and hypercholesterolaemia in hypogonadal men with type 2 diabetes. Eur J Endocrinol 2006;154:899e906.

24. Bhasin S, Woodhouse L, Casaburi R, Singh AB, Bhasin D, Berman N, Chen X, Yarasheski KE, Magliano L, Dzekov C, Dzekov J, Bross R, Phillips J, Sinha-Hikim I, Shen R, Storer TW (2001) Testosterone dose-response relationships in healthy young men. Am J Physiol Endocrinol Metab 281:E1172–1181

25. Laaksonen DE, Niskanen L, Punnonen K, Nyyssnen K, Tuomainen TP, Valkonen VP, et al. Testosterone and sex hormone binding globulin predict the metabolic syndrome and diabetes in middle-aged men. Diabetes Care 2004, 27(5):1036– 1041.

26. Grundy SM. Sex steroid hormones, upper body obesity, and insulin resistance. J Clin Endocrinol

Metab 2002;87(10):4522-4527.

27. Simon C. Testosterone deficiency--the male menopause? InnovAiT 2008;1(9):625-630.

28. Seftel AD, Land S. Testosterone and Cardiovascular Disease. In: Fonseca VA. Cardiovascular Endocrinology. Humana Press;2009:187-197 The Evaluation of Serum Level of Testosterone and Sex Hormone- Binding Globulin in Men with Type 2 Diabetes Mohammad Afkhami–Ardekani*, Laleh Borgian, Javad Mohiti -Ardekani, Zohreh Chiti, Maryam Rashidi, Laila Azod Yazd Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran Received: 21 December, 2009 - Accepted: 9 January, 2010

29.http://www.diabetesselfmanagement.com/Blog/Tara Dairman / low _ testosterone_levels_and_type_2_diabetes/

30. Mooradian AD, Morley JE, Korenman SG (February 1987). "Biological actions of androgens". Endocr. Rev. 8 (1): 1–28. doi:10.1210/edrv-8-1-1. PMID 3549275

31. Svechnikov K, Landreh L, Weisser J, Izzo G, Colón E, Svechnikova I, Söder O (2010). "Origin, development and regulation of human Leydig cells". Horm Res Paediatr. 73 (2): 93–101. doi:10.1159/000277141

32.Guyton TEXTBOOK OF MEDICAL PHYSIOLOGY eleventh edition ISBN 0-7216-0240-1 International Edition ISBN 0-8089-2317-X

33. Ganong Review of medical physiology - 21st ed William F. Ganong, MD

34. Waterman MR, Keeney DS (1992). "Genes involved in androgen biosynthesis and the male phenotype". Horm. Res. 38 (5–6): 217–21. doi:10.1159/000182546.

35.Zuber MX, Simpson ER, Waterman MR (December 1986). "Expression of bovine 17 alpha-hydroxylase cytochrome P-450 cDNA in nonsteroidogenic (COS 1) cells". Science 234 (4781): 1258–61. Bibcode 1986Sci...234.1258Z. doi:10.1126/science.3535074.

36. Harrison's™ PRINCIPLES OF INTERNAL MEDICINE Eighteenth Edition

37. Hammond GL, Bocchinfuso WP (1996). "Sex hormone-binding globulin: gene organization and structure/function analyses". Horm. Res. 45 (3–5): 197–201. doi:10.1159/000184787. PMID 8964583.

38. Ruokonen A, Alén M, Bolton N, Vihko R (July 1985). "Response of serum testosterone and its precursor steroids, SHBG and CBG to anabolic steroid and testosterone self-administration in man". Journal of Steroid Biochemistry 23 (1): 33–8.

39. Bowen, R. (13 May 2004). "Gonadotropins: Luteinizing and Follicle Stimulating Hormones". Colorado State University. Retrieved 12 March 2012.

40. Swerdloff RS, Wang C, Bhasin S (April 1992). "Developments in the control of testicular function". Baillieres Clin. Endocrinol. Metab. 6 (2): 451–83. doi

41. Boulpaep EL, Boron WF (2005). Medical physiology: a cellular and molecular approach. St. Louis, Mo: Elsevier Saunders. pp. 1125. ISBN 1-4160-2328-3.

42. Dickerson LM, Shrader SP, Diaz VA (2008). "Chapter 8: Contraception". In Wells BG, DiPiro JT, Talbert RL, Yee GC, Matzke GR. Pharmacotherapy: a pathophysiologic approach. McGraw-Hill Medical. pp. 1313–28. ISBN 0-07-147899-X.

43.McPhaul MJ, Young M (September 2001). "Complexities of androgen action". J. Am. Acad. Dermatol. 45 (3 Suppl): S87–94. doi:10.1067/mjd.2001.117429.

44. Hiipakka RA, Liao S (October 1998). "Molecular mechanism of androgen action". Trends Endocrinol. Metab. 9 (8): 317–24. doi:10.1016/S1043-2760(98)00081-2.

45. Ross M et al. (2005). "The DNA sequence of the human X chromosome". Nature 434 (7031): 325–37. doi:10.1038/nature03440. PMC 2665286. PMID 15772651.

46. Harper illustrated biochemistry 27th edition.

47. Couse JF, Korach KS. Exploring the role of sex steroids through studies of receptor deficient mice. J Mol Med. 1998 Jun;76(7):497–511. Review

48. Bratoeff E, Cabeza M, Ramirez E, Heuze Y, Flores E (2005). "Recent advances in the chemistry and pharmacological activity of new steroidal antiandrogens and 5 alpha-reductase inhibitors". Curr. Med. Chem. 12 (8): 927–43. doi:10.2174/0929867053507306

49. "Steroid Hormone Receptors and their Response Elements".. Retrieved 2006-11-09.

50. Monty Krieger; Matthew P Scott; Matsudaira, Paul T.; Lodish, Harvey F.; Darnell, James E.; Lawrence Zipursky; Kaiser, Chris; Arnold Berk (2003). Molecular Cell Biology, Fifth Edition. San Francisco: W. H. Freeman. p. 973 pages. ISBN 0-7167-4366-3

51. Swaab DF, Chung WC, Kruijver FP, Hofman MA, Hestiantoro A. Sex differences in the hypothalamus in the different stages of human life. Neurobiol Aging 2003;1:S1-S19

52. Phoenix CH, Goy RW, Gerall AA, Young WC. Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behaviour in the female guinea pig. Endocrinology 1959;65:369-382

53. Swaab DF. Sexual differentiation of the human brain: relevance for gender identity, transsexualism and sexual orientation. Gynecol Endocrinol 2004;19:301-312

54. Langman's Medical Embryology: ninth edition

55. Kubota, Y. et al. The role of insulin 3, testosterone, Müllerian inhibiting substance and relaxin in rat gubernacular growth. Mol. Hum. Reprod. 8, 900-905 (2002).

56.'Male Pattern Baldness', March 01 2010, WebMD: [1]

57.Rebora A (2004). "Pathogenesis of androgenetic alopecia". J Am Acad Dermatol 50 (5): 777–9. doi:10.1016/j.jaad.2003.11.073. PMID 15097964.

58."Hair fiber changes with the development of pattern hair loss". Androgeneticalopecia.com. http://www.androgeneticalopecia.com/hair-loss-biology/hair-loss-fiber-men-women.shtml. Retrieved 2012-11-16.

59. Sex hormones and depth of voice in the male : Meuser W, Nieschlag Dtsch Med Wochenschr. 1977 Feb 25;102(8):261-4.

60. Hatwal A, Singh SK, Agarwal UK, Singh G, Bajpai HS and Gupta SS. Serum testosterone, DHEA-S and androstenedione

levels in acne. Indian Journal of Dermatology, Venereology and Leprology 1990; 56: 427-429.

61. Bhasin S, Storer TW, Berman N, Callegari C, Clevenger B, Phillips J, Bunnell TJ, Tricker R, Shirazi A, Casaburi R (July 1996). "The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men". N. Engl. J. Med. 335 (1): 1–7. doi:10.1056/NEJM199607043350101

62.Kasperk CH, Wergedal JE, Farley JR, Linkhart TA, Turner RT, Baylink DJ. 1989 Androgens directly stimulate proliferation of bone cells in vitro. Endocrinology. 124:1576–1578.

63.Wishner JM, Need AJ, Horowitz M, Morris HA, Nordin BEC. 1995 Effect of age on bone density and bone turnover in men. Clin Endocrinol (Oxf). 42:141–146

64. Tuck SP, Francis RM (2009). "Testosterone, bone and osteoporosis". Front Horm Res. Frontiers of Hormone Research 37: 123–32. doi:10.1159/000176049. ISBN 978-3-8055-8622-1.

65. Effects of testosterone on body composition, bone metabolism and serum lipid profile in middle-aged men: a meta-analysis. (PMID:16117815) Isidori AM, Giannetta E, Greco EA, Gianfrilli D, Bonifacio V, Isidori A, Lenzi A, Fabbri A. Clin. Endocrinol. (Oxf)[2005]

66. http://www.mayoclinic.com/health/testosterone-therapy/MC00030

67.Low Testosterone in Type 2 Diabetes; A Hidden Epidemic?

Evan David Rosen, M.D., Ph.D. Assistant Professor of Medicine, Harvard Medical School addresses another hidden factor in type 2 diabetes. Low Testosterone; A Hidden Epidemic?

68. “Androgen deficiency “Dr. Carolyn Allan MBBS (HONS), DRCOG (UK), FRACP, PhD; Professor Robert I McLachlan MBBS, FRACP, PhD

69.Williams Textbook of Endocrinology . 12th ed. Philadelphia, Pa: Saunders Elsevier; 2011:chap 25.

70.Filippi G. 1986 Klinefelter's syndrome in Sardinia. Clinical report of 265 hypogonadic males detected at the time of military check-up. Clinical Genetics. 30:276-284.

71. "Anorchia". University of Maryland Medical Center. Archived from the original on 6 February 2006

72. Berkowitz GS, Lapinski RH, Dolgin SE, Gazella JG, Bodian CA, Holzman IR. 1993 Prevalence and natural history of cryptorchidism. Pediatrics. 92:44-9.

73. Ringdahl E, Teague L (November 2006). "Testicular torsion". Am Fam Physician 74 (10): 1739–43.

74. Kavoussi, Parviz K.; Costabile, Raymond A. (2011). "Disorders of scrotal contents: orchitis, epididimytis, testicular tortion, tortion of the appendages, and Fournier's gangrene". In Chapple, Christopher R.; Steers, William D.. Practical urology: essential principles and practice. London: Springer-Verlag. ISBN 978-1-84882-033-3.

75. Faiman C. Male hypogonadism. Cleveland Clinic: Current Clinical Medicine. 2nd ed. Philadelphia, Pa: Saunders Elsevier;2010:pgs 397-401.

76. Clinical and hormonal aspects of male hypogonadism in myotonic dystrophy. Mastrogiacomo I, Bonanni G, Menegazzo E, Santarossa C, Pagani E,

Gennarelli M, Angelini C.Source Istituto di Semeiotica Medica, Università di Padova, Italy.

77. Stanworth RD, Jones TH (2008). "Testosterone for the aging male; current evidence and recommended practice". Clin Interv Aging 3 (1): 25–44. PMC 2544367. PMID 18488876

78.Lieblich JM, Rogol AD, White BJ, Rosen SW. 1982 Syndrome of anosmia with hypogonadotropic hypogonadism (Kallmann syndrome). American Journal of Medicine. 73:506-519.

79. Arafah BM. 1986 Reversible hypopituitarism in patients with large nonfunctioning pituitary adenomas. J Clin Endocrinol Metab. 62:1173-9.

80.Charbonnel B, Chupin M, Le Grand A, Guillon J. 1981 Pituitary function in idiopathic haemochromatosis: hormonal study in 36 male patients. Acta Endocrinol (Copenh). 98:178-83.

81.Cohen PG: The hypogonadal-obesity cycle. Med Hypotheses 52:49–51, 1999

82. Enhanced conversion of androstenedione to estrogens in obese males. Kley HK, Deselaers T, Peerenboom H, Krüskemper HL. J Clin Endocrinol Metab. 1980 Nov;51(5):1128-32.

83.Carter JN, Tyson JE, Tolis G, Van Vliet S, Faiman C, Friesen HG. 1978 Prolactin-secreting tumors and hypogonadism in 22 men. N Engl J Med. 299:847-52.

84. AADE : American Association of Diabetes Educators; Men's Health, Low Testosterone and Diabetes: Individualized Treatment and a Multidisciplinary Approach.

85. Margo K, Winn R. Testosterone treatments: why, when, and how? Am Fam Physician. 2006;73:1591-1598.

86.AACE Hypogonadism Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients—2002 update. Endocrine Pract. 2002;8:439-456.

87.Ohl DA, Quallich SA. Clinical hypogonadism and androgen replacement therapy: an overview. Urol Nurs. 2006;26:253-269.

88.Hong BS, Ahn TY. Recent trends in the treatment of testosterone deficiency syndrome. Int J Urol. 2007;14:981-985.

89.Miner MM, Sadovsky R. Evolving issues in male hypogonadism: evaluation, management, and related comorbidities. Cleveland Clin J Med. 2007;74:S38-S46.

90. Wang C, Catlin DH, Demers LM, Starcevic B, Swerdloff RS 2004 Measurement of total serum testosterone in adult men: comparison of current laboratory methods versus liquid chromatography-tandem mass spectrometry. J Clin Endocrinol Metab 89:534–543

91. Winters SJ, Kelley DE, Goodpaster B 1998 The analog free testosterone assay: are the results in men clinically useful? Clin Chem [Erratum (1999) 45:444] 44:2178–2182

92.Morley JE, Patrick P, Perry III HM 2002 Evaluation of assays available to measure free testosterone. Metabolism 51:554–559

93. Rudd BT, Rayner PH, Smith MR, Holder G, Jivani SK, Theodoridis CG. Effect of human chorionic gonadotrophin on plasma and urine testosterone in boys with delayed puberty. Arch Dis Child. 1973 Aug;48(8):590–595.

94. Cacciari E, Cicognani A, Tassoni P, Flamigni P, Bolelli F, Pirazzoli P, Salardi S. Plasma testosterone and estradiol concentration in prepubertal boys with cryptorchidism before and after dexamethasone and after human chorionic gonadotropin administration. Helv Paediatr Acta. 1974 Apr;29(1):27–34.

95.Svartberg J. Epidemiology: testosterone and the metabolic syndrome. Int J Impot Res. 2007;19:124–128. doi: 10.1038/sj.ijir.3901499.

96.Ding EL, Song Y, Malik VS, Liu S. Sex differences of endogenous sex hormones and risk of type 2 diabetes: a systematic review and meta-analysis. Jama. 2006;295:1288–1299. doi: 10.1001/jama.295.11.1288.

97.Zitzmann M, Faber S, Nieschlag E. Association of specific symptoms and metabolic risks with serum testosterone in older men. J Clin Endocrinol Metab. 2006;91:4335–4343. doi: 10.1210/jc.2006-0401.

98. Spark RF. Testosterone, diabetes mellitus, and the metabolic syndrome. Curr Urol Rep. 2007;8:467–471. doi: 10.1007/s11934-007-0050-4.

99.Akishita M, Hashimoto M, Ohike Y, Ogawa S, Iijima K, Eto M, Ouchi Y. Low testosterone level is an independent determinant of endothelial dysfunction in men. Hypertens Res. 2007;30:1029–1034. doi: 10.1291/hypres.30.1029.

100. Kapoor D, Aldred H, Clark S, Channer KS, Jones TH 2007 Clinical and biochemical assessment of hypogonadism in men with type 2 diabetes: correlations with bioavailable testosterone and visceral adiposity. Diabetes Care 30:911–917

101. Despres JP, Lamarche B, Mauriege P, Cantin B, Dagenais GR, Moorjani S, Lupien PJ 1996 Hyperinsulinemia as an independent risk factor for ischemic heart disease. N Engl J Med 334:952–957

102. Selvin E, Feinleib M, Zhang L, Rohrmann S, Rifai N, Nelson WG, Dobs A, Basaria S, Golden SH, Platz EA 2007 Androgens and diabetes in men: results from the Third National Health and Nutrition Examination Survey(NHANES III). Diabetes Care 30:234–238

103. Haffner SM, Karhapaa P, Mykkanen L, Laakso M 1994 Insulin resistance, body fat distribution, and sex hormones in men. Diabetes 43:212–219

104. Thorn LM, Forsblom C, Fagerudd J, Thomas MC, Pettersson-Fernholm K, Saraheimo M, Waden J, Ronnback M, Rosengard-Barlund M, Bjorkesten CG, Taskinen MR, Groop PH 2005 Metabolic syndrome in type 1 diabetes: association with diabetic nephropathy and glycemic control (the FinnDiane study). Diabetes Care 28:2019–2024

105. Laughlin GA, Barrett-Connor E, Bergstrom J. Low serum testosterone and mortality in older men. J Clin Endocrinol Metab 2008;93:68–75.

106. Maggio M, Basaria S. Welcoming low testosterone as a cardiovascular risk factor. Int J Impot Res 2009;21:261–264.

107. Malkin CJ, Pugh PJ, Morris PD, Asif S, Jones TH, Channer KS. Low serum testosterone and increased mortality in men with coronary heart disease. Heart 2010;96:1821–1825.

108. Boyanov MA, Boneva Z, Christov VG. Testosterone supplementation in men with type 2 diabetes, visceral obesity and partial androgen deficiency. Aging Male. 2003;6:1–7. doi: 10.1080/713604734.

109. YialamasMA, Dwyer AA, Hanley E, Lee H, Pitteloud N, Hayes FJ. Acute sex steroid withdrawal reduces insulin sensitivity in healthy men with idiopathic hypogonadotropic hypogonadism. J Clin Endocrinol Metab 2007;92:4254–4259

110. Agledahl I, Hansen JB, Svartberg J. Impact of testosterone treatment on postprandial triglyceride metabolism in elderly men with subnormal testosterone levels. Scand J Clin Lab Invest 2008;68:641–648

111. Lapauw B, Ouwens M, 't Hart LM, et al. Sex steroids affect triglyceride handling, glucose-dependent insulinotropic polypeptide, and insulin sensitivity: a 1-week randomized clinical trial in healthy young men. Diabetes Care 2010;33:1831–1833

112. MacDonald AA, Herbison GP, Showell M, Farquhar CM. The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis. Hum Reprod Update 2010;16:293–311

113 .Mårin P, Holmäng S, Gustafsson C, et al. Androgen treatment of abdominally obese men. Obes Res 1993;1:245–251

114. Maggio M, Basaria S. Welcoming low testosterone as a cardiovascular risk factor. Int J Impot Res 2009;21:261–264

115. Faris JE, Smith MR. Metabolic sequelae associated with androgen deprivation therapy for prostate cancer. Curr Opin Endocrinol Diabetes Obes 2010;17:240–246

116. OLETF (Otsuka Long-Evans Tokushima Fatty) rat: a new NIDDM rat strain. Diabetes Res Clin Pract. 1994 Oct;24 Suppl:S317-20. Kawano K, Hirashima T, Mori S, Natori T.

117. Kupelian V, Shabsigh R, Araujo AB, O'Donnell AB, McKinlay JB. Erectile dysfunction as a predictor of the metabolic syndrome in aging men: results from the Massachusetts Male Aging Study. J Urol 2006;176:222–226

118. Allan CA, McLachlan RI. Androgens and obesity. Curr Opin Endocrinol Diabetes Obes 2010;17:224–232.

119. Brand JS, van der Tweel I, Grobbee DE, Emmelot-Vonk MH, van der Schouw YT. Testosterone, sex hormone-binding globulin and the metabolic syndrome: a systematic review and meta-analysis of observational studies. Int J Epidemiol 2011;40:189–207.

120. Laaksonen DE, Niskanen L, Punnonen K, et al. The metabolic syndrome and smoking in relation to hypogonadism in middle-aged men: a prospective cohort study. J Clin Endocrinol Metab 2005;90:712–719.

121.Corona G, Monami M, Rastrelli G, et al. Type 2 diabetes mellitus and testosterone: a meta-analysis study. Int J Androl. 24 October 2010

122.. Colangelo LA, Ouyang P, Liu K, et al. Association of endogenous sex hormones with diabetes and impaired fasting glucose in men: multi-ethnic study of atherosclerosis. Diabetes Care 2009;32:1049–1051.

123.. Vikan T, Schirmer H, Njølstad I, Svartberg J. Low testosterone and sex hormone-binding globulin levels and high estradiol levels are independent predictors of type 2 diabetes in men. Eur J Endocrinol 2010;162:747–754.

124.Ding EL, Song Y, Manson JE, et al. Sex hormone-binding globulin and risk of type 2 diabetes in women and men. N Engl J Med 2009;361:1152–1163.

125. Keating NL, O'Malley AJ, Freedland SJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy: observational study of veterans with prostate cancer. J Natl Cancer Inst 2010;102:39–46.

126. Mohamed-Ali, V., Goodrick, S., Rawesh, A., Katz, D.R., Miles, J.M., Yudkin, J.S., Klein, S. & Coppack, S.W. (1997) Subcutaneous adipose tissue

releases interleukin-6, but not tumor necrosis factor-alpha, in vivo.Journal of Clinical Endocrinology and Metabolism, 82, 4196–4200.

127. Chaldakov, G.N., Stankulov, I.S., Hristova, M. & Ghenev, P.I. (2003) Adipobiology of disease: adipokines and adipokine-targeted pharmacology. Current Pharmaceutical Design, 9, 1023–1031.

128. Pitteloud N, Hardin M, Dwyer AA, et al. Increasing insulin resistance is associated with a decrease in Leydig cell testosterone secretion in men. J Clin Endocrinol Metab 2005;90:2636–2641.

129. Hamirani YS, Pandey S, Rivera JJ, Ndumele C, Budoff MJ, Blumenthal RS, Nasir K. Markers of inflammation and coronary artery calcification: A systematic review. Atherosclerosis. 2008;201:1–7. doi: 10.1016/j.atherosclerosis.2008.04.045.

130. Malkin CJ, Pugh PJ, Jones RD, Kapoor D, Channer KS, Jones TH. The effect of testosterone replacement on endogenous inflammatory cytokines and lipid profiles in hypogonadal men. J Clin Endocrinol Metab. 2004;89:3313–3318. doi: 10.1210/jc.2003-031069

131. Gooren LJG. Testosterone therapy in aging males and effects on lipid metabolism. Paper presented at: The 4th World Congress on the Aging Male; February 27, 2004; Prague, Czech Republic.

132. Jones RD, Nettleship JE, Kapoor D, et al. Testosterone and atherosclerosis in aging men: purported association and clinical implications. Am J Cardiovasc Drugs 2005;5:141e54.

133. Yildiz O, Seyrek M. Vasodilating mechanisms of testosterone. Exp Clin Endocrinol Diabetes. 2007;115:1–6. doi: 10.1055/s-2007-949657. 134. Malkin CJ, Pugh PJ, Morris PD, et al. Testosterone replacement in hypogonadal men with angina improves ischaemic threshold and quality of life. Heart 2004;90:871e6.

135.Malkin CJ, Pugh PJ, West JN, et al. Testosterone therapy in men with moderate severity heart failure: a double-blind randomized placebo controlled trial. Eur Heart J 2006;27:57e64.

136.van den Beld AW, Muller M, Bots ML, van der Schouw YT, Grobbee DE, Lamberts SWJ. Testosterone and cardiovascular disease, epidemiological aspects.

137.Webb CM, Adamson DL, de Zeigler D, Collins P. Effect of acute testosterone on myocardial ischemia in men with coronary artery disease. Am J Cardiol 1999;83:437–439.

138. English KM, Steeds RP, Jones TH, Diver MJ, Channer KS. Low-dose transdermal testosterone therapy improves angina threshold in men with chronic

stable angina: a randomized, double-blind, placebo-controlled study. Circulation 2000;102:1906–1911.

140. Rolf, C., Kemper, S., Lemmnitz, G., Eickenberg, U. & Nieschlag, E. (2002) Pharmacokinetics of a new transdermal testosterone gel in gonadotropin-suppressed normal men. European Journal of Endocrinology, 146, 673–679.

141.Mårin P, Holmäng S, Gustafsson C, et al. Androgen treatment of abdominally obese men. Obes Res 1993;1:245–251.

142. Heufelder AE, Saad F, Bunck MC, Gooren L. Fifty-two-week treatment with diet and exercise plus transdermal testosterone reverses the metabolic syndrome and improves glycemic control in men with newly diagnosed type 2 diabetes and subnormal plasma testosterone. J Androl 2009;30:726–733.

143. Kalinchenko SY, Tishova YA, Mskhalaya GJ, Gooren LJ, Giltay EJ, Saad F. Effects of testosterone supplementation on markers of the metabolic syndrome and inflammation in hypogonadal men with the metabolic syndrome: the double-blinded placebo-controlled Moscow study. Clin Endocrinol (Oxf) 2010;73:602–612.

144. Farooqi, I.S., Matarese, G., Lord, G.M., Keogh, J.M., Lawrence, E., Agwu, C., Sanna, V., Jebb, S.A., Perna, F., Fontana, S., Lechler, R.I., DePaoli, A.M. & O'Rahilly, S. (2002) Beneficial effects of leptin on obesity, T cell

hyporesponsiveness, and neuroendocrine /metabolic dysfunction of human congenital leptin deficiency. Journal of Clinical Investigation, 110, 1093–1103.

145. Colangelo LA, Ouyang P, Liu K, et al. Association of endogenous sex hormones with diabetes and impaired fasting glucose in men: multi-ethnic study of atherosclerosis. Diabetes Care 2009;32:1049–1051.

146. Phillips GB, Pinkernell BH, Jing TY. The association of hypotestosteronemia with coronary artery disease in men. Arterioscler Thromb 1994;14:701–6.

147. Jones TH, Arver S, Behre HM, et al Testosterone replacement in hypogonadal men with type 2 diabetes and/or metabolic syndrome (The TIMES2 Study). Diabetes Care 2011;34:828–837 pmid :21386088

148.Coviello AD, Kaplan B, Lakshman KM, Chen T, Singh AB, Bhasin S: Effects of graded doses of testosterone on erythropoiesis in healthy young and older men. J Clin Endocrinol Metab 2008, 93(3):914-919.

149.Tivesten A, Mellstrom D, Jutberger H, Fagerberg B, Lernfelt B, Orwoll E, Karlsson MK, Ljunggren O, Ohlsson C: Low serum testosterone and high serum estradiol associate with lower extremity peripheral arterial disease in elderly men. The MrOS Study in Sweden. J Am Coll Cardiol 2007, 50(11):1070-1076.

150.Webb CM, Elkington AG, Kraidly MM, Keenan N, Pennell DJ, Collins P: Effects of oral testosterone treatment on myocardial perfusion and vascular function in men with low plasma testosterone and coronary heart disease. Am J Cardiol 2008,101(5):618-624.

151. Zitzmann M, Brune M, Nieschlag E: Vascular reactivity in hypogonadal men is reduced by androgen substitution. J Clin Endocrinol Metab 2002, 87(11):5030-5037.

152. Guay A, Jacobson J: The relationship between testosterone levels, the metabolic syndrome (by two criteria), and insulin resistance in a population of men with organic erectile dysfunction. J Sex Med 2007, 4(4 Pt 1):1046-1055.

153. Bhasin S, Calof OM, Storer TW, Lee ML, Mazer NA, Jasuja R, Montori VM, Gao W, Dalton JT: Drug insight: Testosterone and selective androgen receptor modulators as anabolic therapies for chronic illness and aging. Nat Clin Pract Endocrinol Metab 2006, 2(3):146-159.

154. Li S, Li X, Li J, Deng X, Li Y: Inhibition of oxidative-stressinduced platelet aggregation by androgen at physiological levels via its receptor is associated with the reduction of thromboxane A2 release from platelets. Steroids 2007, 72(13):875-880.

155. Bhatt DL: Anti-inflammatory agents and antioxidants as a possible "third great wave" in cardiovascular secondary prevention. Am J Cardiol 2008, 101(10A):4D-13D.

156. Norata GD, Tibolla G, Seccomandi PM, Poletti A, Catapano AL:

Dihydrotestosterone decreases tumor necrosis factor-alpha and lipopolysaccharide-induced inflammatory response in human endothelial cells. J Clin Endocrinol Metab 2006, 91(2):546-554.

PATIENT CONSENT FORM

STUDY DETAIL

"STUDY OF TESTOSTERONE LEVELS IN MEN WITH TYPE 2 DIABETES MELLITUS"

STUDY CENTRE : Chengalpattu Medical College and Government General Hospital.

PATIENTS NAME :

PATIENTS AGE :

IDENTIFICATION NUMBER :

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression:

Patients Name and Address: Place Date

Signature of investigator :

Study investigator's Name : Place Date

MASTER CHART- DIABETICS

S.No.	Name	Age	Sex	OP No.	D.O.S.	Duration of DM	Ass other RISK FACTORS	PR	BP (mm/Hg)	CVS	RS	CNS	BMI	W/H ratio	CBC		
															Hb (g/dl)	TC (/cu.mm)	DC
1	Subramani	47yrs	M	1719/11	02-04-2012	3yrs	NIL	86	120/80	N	N	N	20.8	0.82	16.2	4120	53/42/5
2	Veeramani	35yrs	M	2362/11	02-04-2012	3yrs	NIL	88	110/70	N	N	N	23.03	0.85	13.6	5500	70/28/2
3	Hariraman	38yrs	M	2037/12	02-04-2012	6months	NIL	72	130/80	N	N	N	25.2	0.96	14.5	6300	67/30/3
4	Meganathan	36yrs	M	2043/12	02-04-2012	11/2 yrs	NIL	86	120/70	N	N	N	19.5	0.78	12.8	7500	60/38/2
5	Gunasekar	57yrs	M	589/07	02-04-2012	15yrs	HTN	90	120/80	N	N	N	20.68	0.81	14.7	4340	72/27/1
6	Thambiraj	75yrs	M	753/10	02-04-2012	2yrs	NIL	82	120/80	N	N	N	26.8	0.97	13.7	6700	76/22/2
7	Ellapan	52yrs	M	2040/12	02-04-2012	4yrs	HTN	80	90/60	N	N	N	25.24	0.96	14.6	7800	71/26/3
8	Mani	50yrs	M	1696/12	02-04-2012	6months	NIL	96	120/80	N	N	N	22.8	0.84	16	6000	70/26/4
9	Elumalai	52yrs	M	19/2011	16-04-2012	6yrs	CAD	80	130/80	N	N	N	27.8	0.98	15.7	4700	60/39/1
10	Anamalai	55yrs	M	1315/09	16-04-2012	3yrs	HTN	88	120/80	N	N	N	22.22	0.86	14.2	4120	53/42/5
11	Venkatesan	65yrs	M	169/02	16-04-2012	10yrs	CAD/HTN	90	100/70	N	N	N	37.25	1.33	13.8	7500	60/38/2
12	Elangovan	48yrs	M	89/05	16-04-2012	20yrs	CAD/HTN	86	110/80	N	N	N	21.77	0.82	11.7	4340	72/27/1
13	Susairaj	60yrs	M	1175/06	16-04-2012	10yrs	HTN	82	100/60	N	N	N	30.9	1.02	9.2	4120	53/42/5
14	Paranjothi	68yrs	M	160/03	16-04-2012	9yrs	NIL	72	130/90	N	N	N	20.8	0.81	13.7	6700	76/22/2
15	Ramanujam	48yrs	M	1592/11	16-04-2012	1yr	NIL	88	90/60	N	N	N	23.3	0.89	11.6	7800	71/26/3
16	Arun	38yrs	M	2047/12	16-04-2012	6months	NIL	82	130/90	N	N	N	25.2	0.96	13.4	4500	68/30/2
17	Satish	40yrs	M	2015/12	07-05-2012	1yr	NIL	88	120/80	N	N	N	25.7	0.98	13	6800	75/23/2
18	Subbaih	55yrs	M	568/05	07-05-2012	8yrs	CAD/HTN	72	110/70	N	N	N	31.5	1.12	10.3	9000	74/23/3
19	Ramu	46yrs	M	2045/12	07-05-2012	6months	NIL	78	90/60	N	N	N	25.6	0.98	10.2	6370	60/31/3
20	Verumandi	63yrs	M	160/01	07-05-2012	17yrs	CAD/HTN	80	120/80	N	N	N	20.8	0.82	11.3	4390	56/40/4
21	Madasamy	53yrs	M	1496/09	07-05-2012	4yrs	NIL	88	100/70	N	N	N	23.5	0.89	11.4	6370	49/48/3
22	Veeraiyan	55yrs	M	1568/09	07-05-2012	5yrs	HTN	84	100/60	N	N	N	25.8	0.98	10.8	7500	60/38/2
23	Ramaiah	65yrs	M	562/02	07-05-2012	14yrs	CAD	90	110/80	N	N	N	27.6	1.1	11.8	7450	68/31/1
24	Ponnaiyan	54yrs	M	1150/10	07-05-2012	4yrs	HTN	78	140/70	N	N	N	24.1	0.91	14	7100	60/34/1
25	Abdulkhadar	46yrs	M	2030/12	21-05-2012	6months	NIL	80	110/80	N	N	N	23.8	0.89	12.5	9400	75/24/1
26	Suresh	45yrs	M	2053/12	21-05-2012	2yrs	NIL	72	110/70	N	N	N	22.6	0.86	11.6	8390	73/26/1
27	Antony	58yrs	M	1048/04	21-05-2012	8yrs	NIL	86	110/70	N	N	N	24.8	0.92	10.8	7500	60/38/2
28	Basker	64yrs	M	584/01	21-05-2012	15yrs	NIL	88	120/80	N	N	N	20.1	0.84	11.4	6370	49/48/3
29	Ramalingam	70yrs	M	894/03	21-05-2012	16yrs	HTN	92	90/60	N	N	N	20.3	0.83	10.3	9000	74/23/3
30	Arunachalam	53yrs	M	620/09	21-05-2012	4yrs	CAD/HTN	84	130/80	N	N	N	33.4	0.98	13.6	7800	68/29/3
31	Balu	44yrs	M	1184/11	21-05-2012	2yrs	NIL	86	140/90	N	N	N	22.45	0.86	10.8	7500	60/38/2
32	Veerasamy	72yrs	M	144/01	21-05-2012	20yrs	CAD	86	130/80	N	N	N	23.02	0.86	11.4	6370	49/48/3
33	Kani	47yrs	M	1050/11	04-06-2012	2yrs	NIL	88	120/80	N	N	N	34.5	1.15	10.3	4100	62/34/4
34	Sekar	58yrs	M	956/05	04-06-2012	7yrs	NIL	86	140/90	N	N	N	32.1	0.99	13	5500	65/32/3
35	Muthu	65yrs	M	546/03	04-06-2012	17yrs	CAD/HTN	86	130/80	N	N	N	20.3	0.82	12.8	4700	74/24/1
36	Ragavan	60yrs	M	1145/02	04-06-2012	10yrs	NIL	90	120/60	N	N	N	23.33	0.91	14	7100	60/34/1
37	Vinoth	38yrs	M	2016/12	04-06-2012	1yr	NIL	78	140/70	N	N	N	22.8	0.92	13.6	7800	68/29/3
38	Jeeva	40yrs	M	2095/11	04-06-2012	2yrs	NIL	88	130/80	N	N	N	24.5	0.93	10.8	7500	60/38/2
39	Arul	46yrs	M	2072/12	04-06-2012	1yr	NIL	84	110/70	N	N	N	28.8	0.99	11.4	6370	49/48/3
40	Nandhakumar	49yrs	M	2002/11	04-06-2012	3yrs	NIL	100	120/80	N	N	N	28.6	0.98	13.5	9000	55/47/3
41	Divan	42yrs	M	2044/11	18-06-2012	2yrs	NIL	72	110/70	N	N	N	25.6	0.96	9.8	6110	70/26/4
42	Sundar	46yrs	M	726/11	18-06-2012	2yrs	NIL	78	140/70	N	N	N	23.3	0.89	10.8	7500	60/38/2
43	Vinayagam	57yrs	M	693/03	18-06-2012	12yrs	CAD/HTN	72	110/70	N	N	N	29.2	1.1	11.4	6370	49/48/3
44	Mayilsami	50yrs	M	926/10	18-06-2012	3yrs	NIL	80	110/80	N	N	N	24.2	0.92	13	5500	65/32/3
45	Harichandran	47yrs	M	2026/12	18-06-2012	8months	NIL	84	110/70	N	N	N	22.1	0.89	13.6	8050	67/31/2
46	Gopal	42yrs	M	2028/12	18-06-2012	2yrs	NIL	86	130/80	N	N	N	20.6	0.89	12.2	7390	66/32/2
47	Balan	46yrs	M	2101/12	18-06-2012	1yr	NIL	80	120/80	N	N	N	21.4	0.84	12	8000	68/30/2
48	Yogaraj	65yrs	M	132/01	18-06-2012	20yrs	CAD/HTN	88	110/70	N	N	N	32.2	1.24	11.6	7600	75/24/1
49	Sukumar	48yrs	M	821/11	02-07-2012	2yrs	NIL	92	120/80	N	N	N	31.75	1.1	10.8	7500	60/38/2

S.No.	Name	Age	Sex	OP No.	D.O.S.	Duration of DM	Ass other RISK FACTORS	PR	BP (mm/Hg)	CVS	RS	CNS	BMI	W/H ratio	CBC		
50	Mohan	38yrs	M	2094/12	02-07-2012	6months	NIL	64	110/70	N	N	N	19.2	0.79	10.3	9000	74/23/3
51	Govindaraj	52yrs	M	256/10	02-07-2012	3yrs	NIL	86	110/80	N	N	N	22.4	0.85	13.6	7800	68/29/3
52	Selvaraj	54yrs	M	1041/07	02-07-2012	6yrs	CAD/HTN	74	110/70	N	N	N	25.8	0.96	13	5500	65/32/3
53	Muniyappan	57yrs	M	1542/04	02-07-2012	10yrs	HTN	88	110/70	N	N	N	20.68	0.86	13.8	6110	70/26/4
54	Chinnapaji	52yrs	M	1458/09	02-07-2012	4yrs	HTN	92	100/60	N	N	N	26.33	0.98	11.6	5890	72/27/1
55	Muthaal	55yrs	M	1552/09	02-07-2012	7yrs	CAD/HTN	80	120/70	N	N	N	28.5	0.99	13.6	7800	68/29/3
56	Deivendran	49yrs	M	2014/12	02-07-2012	1yr	NIL	92	120/80	N	N	N	24.24	0.89	12.8	7500	60/38/2
57	Selvakumar	60yrs	M	188/01	23-07-2012	20yrs	CAD/HTN	70	100/70	N	N	N	27.45	1.1	13.5	9000	55/47/3
58	Pushparaj	54yrs	M	1428/07	23-07-2012	6yrs	CAD/HTN	72	110/60	N	N	N	34.5	1.15	12.3	6110	70/26/4
59	Arumugam	64yrs	M	147/02	23-07-2012	15yrs	NIL	86	110/80	N	N	N	28.4	0.99	14.6	8000	70/28//2
60	Venugopal	55yrs	M	356/04	23-07-2012	10yrs	CAD	76	100/60	N	N	N	23.22	0.86	15.6	4100	76/20/4
61	Kandasamy	55yrs	M	1550/09	23-07-2012	5yrs	HTN	84	110/80	N	N	N	22.22	0.84	14.8	9840	60/36/4
62	Vijayan	45yrs	M	265/11	23-07-2012	2yrs	NIL	90	110/70	N	N	N	24.18	0.92	16.2	9000	60/38/2
63	Tamilselvan	55yrs	M	1520/07	23-07-2012	6yrs	HTN	86	110/70	N	N	N	23.65	0.89	14	5647	71/27/2
64	Senthil	52yrs	M	251/09	23-07-2012	4yrs	HTN/CAD	78	120/80	N	N	N	32.5	0.99	13.6	7800	68/29/3
65	Paranthaman	52yrs	M	118/02	13-08-2012	15yrs	CAD/HTN	72	90/60	N	N	N	20.78	0.87	14.8	7500	60/38/2
66	Kalaiselvan	54yrs	M	596/05	13-08-2012	10yrs	CAD	80	130/80	N	N	N	31.75	1.1	15.5	6110	70/26/4
67	Siva	45yrs	M	1849/09	13-08-2012	5yrs	HTN	84	140/90	N	N	N	30.25	0.98	13.4	9840	60/36/4
68	Rajaram	48yrs	M	2030/12	13-08-2012	1yr	NIL	86	130/80	N	N	N	21.5	0.86	14.4	7500	60/38/2
69	Gopikannan	65yrs	M	125/01	13-08-2012	16yrs	HTN	80	120/80	N	N	N	24.34	0.92	15.8	6110	70/26/4
70	Inbaraj	50yrs	M	1750/09	13-08-2012	5yrs	HTN	88	140/90	N	N	N	26.4	0.98	13.2	9150	57/42/1
71	Dhanavel	52yrs	M	1658/09	13-08-2012	5yrs	HTN	92	130/80	N	N	N	28.33	0.99	11.8	8800	69/29/2
72	Poovaraghavan	55yrs	M	155/09	13-08-2012	6yrs	CAD	72	120/60	N	N	N	27.5	0.96	13.6	5600	68/30/2
73	Manoharan	51yrs	M	1456/10	27-08-2012	3yrs	NIL	68	140/70	N	N	N	23.33	0.86	15.2	6250	62/36/2
74	Velayuthan	50yrs	M	152/10	27-08-2012	4yrs	NIL	76	130/80	N	N	N	23.02	0.89	13.5	5800	75/24/1
75	Solomon	51yrs	M	1650/09	27-08-2012	5yrs	HTN	92	110/70	N	N	N	28.4	1.1	16.2	9800	76/23/1
76	Rambabu	60yrs	M	254/01	27-08-2012	14yrs	NIL	84	120/80	N	N	N	24.1	0.92	12.8	7900	71/27/2
77	Sathyanarayanan	55yrs	M	148/09	27-08-2012	4yrs	HTN	90	110/70	N	N	N	22.6	0.84	15.8	9520	70/26/4
78	Kasinathan	50yrs	M	1758/10	27-08-2012	3yrs	NIL	88	120/80	N	N	N	22.64	0.89	13.8	6000	60/38/2
79	Saravanan	48yrs	M	2541/12	27-08-2012	1yr	NIL	72	110/70	N	N	N	25.9	0.96	15.3	8500	58/42/0
80	Balakrishanan	60yrs	M	132/01	27-08-2012	16yrs	NIL	84	130/80	N	N	N	27.42	0.98	14	5100	62/37/1
81	Narayanan	50yrs	M	2150/12	10-09-2012	2yrs	HTN	76	120/70	N	N	N	20.12	0.88	13.6	9750	72/26/2
82	Mahendran	65yrs	M	146/03	10-09-2012	15yrs	HTN	86	120/80	N	N	N	19.5	0.79	12.7	9300	70/25/5
83	Periyasami	75yrs	M	896/03	10-09-2012	20yrs	NIL	74	120/80	N	N	N	27.7	0.99	15.2	5600	77/22/1
84	Chellaiyan	56yrs	M	564/04	10-09-2012	10yrs	NIL	78	90/60	N	N	N	32.75	1.1	13.8	6800	71/26/3
85	Nallamuthu	50yrs	M	1586/10	10-09-2012	3yrs	HTN	72	120/80	N	N	N	23.03	0.88	14.6	7400	67/32/1
86	Kathirvel	48yrs	M	1678/12	10-09-2012	1yr	NIL	80	130/80	N	N	N	19.8	0.84	16.2	7100	75/22/3
87	Sambantham	75yrs	M	1584/05	10-09-2012	17yrs	NIL	84	120/80	N	N	N	24.5	0.92	13.5	9300	60/37/3
88	Rajadurai	64yrs	M	1426/05	10-09-2012	10yrs	NIL	86	100/70	N	N	N	22.8	0.89	14	6500	72/26/2
89	Ganesh	62yrs	M	1326/09	24-09-2012	5yrs	NIL	80	110/80	N	N	N	21.4	0.87	13.6	7550	67/31/2
90	Vadivel	45yrs	M	2147/12	24-09-2012	8months	NIL	88	100/60	N	N	N	20.78	0.84	12.8	7600	60/36/4
91	Kannan	62yrs	M	196/01	24-09-2012	18yrs	HTN/CAD	92	130/90	N	N	N	21.77	0.92	14.6	10500	72/25/3
92	Velu	55yrs	M	1245/04	24-09-2012	10yrs	CAD/HTN	66	120/90	N	N	N	32.25	1.25	13.8	4550	76/22/2
93	Vignesh	55yrs	M	1457/09	24-09-2012	5yrs	HTN	86	130/90	N	N	N	28.66	0.99	14.2	9750	72/27/1
94	Mahadevan	50yrs	M	215/10	24-09-2012	3yrs	CAD/HTN	88	130/80	N	N	N	25.8	0.96	13.6	8500	70/28/2
95	Rajakumar	72yrs	M	214/05	24-09-2012	10yrs	CAD	80	120/90	N	N	N	24.51	0.91	14.8	6000	60/38/2
96	Jeyakumar	56yrs	M	1632/09	24-09-2012	5yrs	NIL	86	110/70	N	N	N	22.6	0.88	15.4	9550	68/32/0
97	Thirunavukarsu	65yrs	M	456/01	24-09-2012	15yrs	NIL	72	120/80	N	N	N	26.8	0.97	16	7800	70/26/4
98	Gopi	60yrs	M	895/03	24-09-2012	11yrs	NIL	76	130/90	N	N	N	20.5	0.86	14.2	8500	60/38/2
99	Ramamoorthy	50yrs	M	1876/09	24-09-2012	5yrs	HTN	90	120/90	N	N	N	26.5	0.99	13.8	7400	69/30/1
100	Elumalai	62yrs	M	159/02	24-09-2012	12yrs	CAD	86	110/70	N	N	N	27.8	1.15	12.8	8400	70/29/1

PL (lak/cu. mm)
1.2
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2.54
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2.8
2.6

LFT					RFT						TOT CHOLESTROL(mg/dl)	HIV	Serum Total TESTOSTERONE (ng/dl)
TB (mg/dl)	DB (mg/dl)	OT (IU/L)	PT (IU/L)	TP (g/dl)	FBS (mg/dl)	PPBS (mg/dl)	Urea (mg/dl)	Creatine (mg/dl)	Na (meq/L)	K (meq/L)			
1	0.4	24	36	6	147	222	44	1.5	134	4	170	negative	424
0.9	0.3	16	27	6.5	110	140	25	0.9	141	4.5	166	negative	617
1	0.3	21	35	8.2	128	152	40	1.2	142	3.5	180	negative	312
0.9	0.2	26	29	7	169	200	42	1.4	138	3.9	188	negative	302
0.8	0.3	28	35	6.8	126	148	46	1.5	144	3.5	210	negative	343
0.9	0.4	28	29	6.9	116	140	26	1.4	134	4	238	negative	120
0.8	0.2	25	30	6.9	176	220	55	2.1	135	3.5	200	negative	302
0.8	0.2	30	35	5.8	76	134	40	1.2	141	4.5	190	negative	467
0.9	0.3	20	22	6.4	128	150	22	0.6	136	3.6	220	negative	267
1	0.4	24	36	6	147	210	44	1.2	134	4	215	negative	232
0.9	0.2	26	29	7	139	200	30	1	138	3.9	260	negative	184
0.8	0.3	28	35	6.8	165	232	46	1.6	144	3.5	225	negative	277
1	0.4	24	36	6	120	157	21	0.7	134	4	242	negative	287
0.9	0.4	28	29	6.9	176	240	54	1.8	134	4	190	negative	316
0.8	0.2	25	30	6.9	164	210	44	1.6	135	3.5	160	negative	458
1	0.4	26	24	6.4	128	160	24	0.9	140	4	155	negative	756
0.9	0.3	27	32	7	120	165	40	1.2	139	3.9	170	negative	352
0.8	0.3	23	30	6.5	144	198	46	1.4	130	3	250	negative	189
0.7	0.2	25	35	6.3	155	215	23	0.9	146	4	166	negative	525
0.8	0.2	29	31	6.6	104	130	48	1.4	140	3.8	190	negative	178
0.9	0.3	24	29	6.2	128	163	44	1.2	145	3.9	170	negative	334
0.9	0.2	26	29	7	169	230	50	1.1	138	3.9	250	negative	219
0.9	0.2	21	27	6.6	114	135	28	1	138	4.7	230	negative	264
0.9	0.3	27	31	6.6	130	160	40	1.2	133	3.5	225	negative	270
1.2	0.3	24	33	5.9	92	134	24	1	135	3.5	180	negative	415
1.2	0.3	30	44	6.5	110	140	40	1.2	140	4.7	177	negative	418
0.9	0.2	26	29	7	135	180	30	1	138	3.9	200	negative	425
0.9	0.3	24	29	6.2	120	155	44	1.2	145	3.9	160	negative	326
0.8	0.3	23	30	6.5	124	160	49	1.4	130	3.4	210	negative	224
0.6	0.1	22	27	6.2	116	140	37	1	137	3.7	255	negative	202
0.9	0.2	26	29	7	160	200	48	1.5	138	3.9	175	negative	402
0.9	0.3	24	29	6.2	155	189	44	1.2	145	3.9	220	negative	202
0.8	0.2	20	31	6.2	140	210	50	1.1	145	4.8	250	negative	337
1	0.3	26	29	6.6	180	250	28	0.8	143	4	200	negative	468
0.9	0.3	24	29	6.1	100	139	30	0.9	138	4.1	238	negative	185
0.9	0.3	27	31	6.6	119	140	42	1.1	133	3.5	180	negative	357
0.6	0.1	22	27	6.2	130	160	47	1.4	137	3.7	160	negative	512
0.9	0.2	26	29	7	147	200	50	1.8	138	3.9	170	negative	434
0.9	0.3	24	29	6.2	116	136	44	1.2	145	3.9	175	negative	330
0.7	0.2	27	31	7.4	98	130	28	0.9	141	4.2	220	negative	254
0.8	0.2	21	16	6.4	132	170	31	1.2	140	3.1	180	negative	312
0.9	0.2	26	29	7	125	156	30	1.1	138	3.9	165	negative	345
0.9	0.3	24	29	6.2	148	200	44	1.2	145	3.9	230	negative	120
1	0.3	26	29	6.6	162	220	46	1.5	143	4	190	negative	264
1.5	0.5	23	33	7	126	160	26	0.9	143	3.8	160	negative	524
0.8	0.2	40	48	6.2	105	140	47	1.2	144	3.4	166	negative	545
0.9	0.4	28	30	6.5	110	132	30	0.6	146	3.8	170	negative	502
0.9	0.3	24	35	6.9	148	215	48	1.2	139	4	260	negative	160
0.9	0.2	26	29	7	136	174	40	1.4	138	3.9	265	negative	178

LFT					RFT						TOT CHOLESTROL(mg/dl)	HIV	Serum Total TESTOSTERONE (ng/dl)
0.8	0.3	23	30	6.5	124	165	39	1	130	3.4	150	negative	828
0.6	0.1	22	27	6.2	106	140	37	0.9	137	3.7	160	negative	407
1	0.3	26	29	6.6	114	132	28	0.8	143	4	220	negative	225
0.8	0.2	21	16	6.4	135	154	40	1.1	140	3.1	215	negative	304
0.9	0.2	25	30	7.5	140	186	44	1.6	144	4.1	210	negative	412
0.6	0.1	22	27	6.2	105	134	37	0.8	137	3.7	220	negative	202
0.9	0.2	26	29	7	122	156	30	0.7	138	3.9	170	negative	408
0.7	0.2	27	31	7.4	120	160	28	0.9	141	4.2	224	negative	120
0.8	0.2	21	16	6.4	110	144	31	1	140	3.1	255	negative	164
1	0.3	34	44	6.5	186	290	40	1.5	148	3.7	200	negative	342
0.9	0.3	59	68	6.4	155	240	42	1.2	137	3.8	236	negative	192
1	0.3	28	35	6.9	110	154	28	1	140	3.3	248	negative	300
0.8	0.2	34	54	6	132	166	48	1.6	140	4	180	negative	344
0.9	0.3	27	36	6.6	118	140	27	0.8	137	4.1	210	negative	315
0.6	0.1	22	27	6.2	106	136	37	0.6	137	3.7	238	negative	170
0.9	0.2	26	29	7	140	180	40	1.2	138	3.9	250	negative	120
0.8	0.2	21	16	6.4	136	164	31	1	140	3.1	220	negative	122
1	0.3	28	35	6.9	110	152	28	0.9	140	3.3	200	negative	322
0.9	0.2	26	29	7	106	143	30	0.7	138	3.9	180	negative	386
0.8	0.2	21	16	6.4	126	140	40	1.1	140	3.1	200	negative	338
1	0.4	24	35	6	124	165	31	0.9	144	4	260	negative	178
0.9	0.3	16	22	6.5	136	180	44	1.5	146	4.5	210	negative	315
1	0.3	21	36		148	198	40	1.2	139	3.5	220	negative	260
0.9	0.2	26	29	7	156	210	40	1.4	138	3.9	175	negative	424
0.8	0.3	28	35	6.8	100	136	28	0.8	130	3.5	190	negative	319
0.9	0.4	28	36	6.9	118	142	27	0.8	137	4	250	negative	206
0.8	0.2	25	29	6.9	104	136	37	1	143	3.5	220	negative	230
0.8	0.2	30	30	5.8	146	190	44	1.5	140	4.5	225	negative	285
0.9	0.3	20	24	6.4	112	130	31	0.8	144	3.6	170	negative	408
1	0.4	24	32	6	90	124	28	0.9	137	4	230	negative	298
0.9	0.2	26	30	7	120	148	30	0.7	138	3.9	224	negative	228
0.8	0.3	28	35	6.8	110	152	40	1	141	3.5	168	negative	428
1	0.4	24	31	6	104	130	37	1	140	4	200	negative	263
0.9	0.4	28	29	6.9	134	176	44	1.2	148	4	238	negative	140
0.8	0.2	25	29	6.9	180	250	48	1.8	137	3.5	242	negative	202
1	0.4	26	27	6.4	128	158	28	1	140	4	165	negative	400
0.9	0.3	27	31	7	110	146	30	1.1	140	3.9	163	negative	480
0.8	0.3	30	33	6.5	100	132	31	0.8	137	3	230	negative	226
0.9	0.2	20	44	6.2	114	138	44	1.2	143	4	215	negative	260
0.8	0.2	24	29	7	110	144	40	1.2	140	3.1	200	negative	384
0.8	0.3	26	29	7.4	124	159	38	1	144	3.7	160	negative	506
0.9	0.4	28	30	6.4	130	176	28	0.9	137	3.8	250	negative	198
1	0.4	24	27	6.5	148	200	44	1.4	138	3.3	230	negative	190
0.9	0.2	28	29	6.4	110	162	31	1	141	4	200	negative	307
0.8	0.4	25	29	6.9	120	155	37	0.9	140	4.1	192	negative	258
0.9	0.3	26	31	6	140	180	40	1.2	137	3.7	230	negative	250
0.6	0.2	27	29	6.6	124	156	42	1.2	138	3.9	200	negative	412
0.9	0.2	28	29	6	110	140	28	0.9	141	4.2	210	negative	218
0.7	0.3	24	31	7	120	145	30	0.8	140	3.8	215	negative	179
0.8	0.3	28	14	6.8	100	132	31	0.8	148	4	236	negative	189
0.6	0.1	16	18	7.8	160	196	31	1.4	147	4.3	230	negative	245

MASTER CHART NON DIABETICS

S.No.	Name	Age	Sex	OP No.	D.O.S.	Duration of DM	PR	BP (mm/Hg)	CVS	RS	CNS	BMI	W/H ratio	CBC				RFT					
														Hb (g/dl)	TC (/cu.mm)	DC	PL (lak/cu. mm)	RBS	Urea	Creatine	Na	K	TB (mg/dl)
1	Diwakar	40yrs	M	56586	06-04-2012	NIL	86	120/80	N	N	N	21.4	0.84	14.2	6560	72/27/2	1.38	132	26	0.8	145	3.9	0.9
2	Jegadeesan	35yrs	M	50281	06-04-2012	NIL	88	110/70	N	N	N	22.4	0.84	15.6	7500	70/28/2	2.5	109	30	1	143	3.8	0.8
3	Chinnamani	43yrs	M	51902	06-04-2012	NIL	72	130/80	N	N	N	20.4	0.076	12.6	6832	67/30/3	2.5	121	28	1	140	4	1
4	Venkatesan	45yrs	M	56570	06-04-2012	NIL	86	120/70	N	N	N	22.4	0.86	13.5	7700	60/38/2	2	113	34	1.2	135	3.5	0.7
5	Jayaraman	40yrs	M	53584	13-04-2012	NIL	90	120/80	N	N	N	23.5	0.96	15.2	4675	72/27/1	2.7	120	20	0.6	145	3.9	0.9
6	Soundaraj	42yrs	M	54598	13-04-2012	NIL	82	120/80	N	N	N	20.2	0.82	13.6	6800	76/22/2	2	92	19	0.9	146	4.2	1
7	Kumar	38yrs	M	56521	13-04-2012	NIL	80	90/60	N	N	N	20.6	0.86	14.2	7900	71/26/3	1.2	78	26	1	145	3.5	0.7
8	Suresh	40yrs	M	52551	13-04-2012	NIL	96	120/80	N	N	N	21.4	0.9	16.1	6200	70/26/4	1.01	65	40	1	134	4.5	0.8
9	Mani	44yrs	M	58722	20-04-2012	NIL	80	130/80	N	N	N	21.8	0.8	12.9	4800	60/39/1	4	128	30	0.7	138	3.8	0.9
10	Sekar	45yrs	M	58572	20-04-2012	NIL	88	120/80	N	N	N	19.6	0.83	14.2	4500	53/42/5	1.6	128	26	0.8	143	3.5	0.9
11	Karthick	41yrs	M	58890	20-04-2012	NIL	90	100/70	N	N	N	23.4	1.1	15.2	7800	60/38/2	1.47	108	32	1	140	3.5	0.8
12	Natesan	45yrs	M	58907	20-04-2012	NIL	86	110/80	N	N	N	23.2	0.91	13.4	4545	72/27/1	2.6	72	20	0.7	120	4	1
13	Thambiah	45yrs	M	69860	27-04-2012	NIL	82	100/60	N	N	N	29.2	1.1	14.5	4500	53/42/5	1.4	128	22	0.8	135	3	1
14	Rajkumar	48yrs	M	65985	27-04-2012	NIL	72	130/90	N	N	N	20.1	0.7	15.3	4700	76/22/2	1.38	127	28	0.9	138	3.5	0.8
15	Manikumar	52yrs	M	68157	27-04-2012	NIL	88	90/60	N	N	N	28.6	1.02	13.6	7700	71/26/3	2.2	32	26	0.9	138	3.5	0.9
16	Damodharan	55yrs	M	69980	27-04-2012	NIL	82	130/90	N	N	N	31.2	1.2	12.4	4700	68/30/2	2.8	90	28	1	143	4.3	0.7
17	Prathab	46yrs	M	69866	04-05-2012	NIL	88	120/80	N	N	N	20.4	0.9	12.8	6700	75/23/2	3.2	128	44	1.2	146	3.5	1
18	Sundaram	48yrs	M	71228	04-05-2012	NIL	72	110/70	N	N	N	22.4	0.91	14.3	9000	74/23/3	1.01	124	39	1.4	130	3	0.8
19	Gyansingh	50yrs	M	74880	04-05-2012	NIL	78	90/60	N	N	N	21.6	0.8	12.2	4395	67/31/2	1.5	100	44	1.2	145	3.9	0.8
20	Murali	53yrs	M	70652	04-05-2012	NIL	80	120/80	N	N	N	29.4	1.2	12.4	4390	56/40/4	1.2	109	38	0.7	138	4	0.8
21	Gandhi	50yrs	M	76023	11-05-2012	NIL	88	100/70	N	N	N	20.4	0.81	15.3	6570	49/48/3	1.7	120	42	1.1	140	3.6	0.9
22	Yusuf	55yrs	M	71252	11-05-2012	NIL	84	100/60	N	N	N	29.4	1.02	16	7600	60/38/2	1.48	110	32	1	144	3.7	0.9
23	Veeraraghavan	50yrs	M	76145	11-05-2012	NIL	90	110/80	N	N	N	19.7	0.78	15.2	7500	68/31/1	3.2	122	32	1.1	140	4.7	1.2
24	Kumaresan	54yrs	M	72912	11-05-2012	NIL	78	140/70	N	N	N	26.2	0.92	13.4	7200	65/35/0	1.46	120	44	1.2	138	3.6	0.9
25	Surendar	51yrs	M	74510	18-05-2012	NIL	80	110/80	N	N	N	25.4	1.1	13	9600	75/24/1	1.32	94	30	1	135	3.5	1.2
26	Murugasen	54yrs	M	71228	18-05-2012	NIL	72	110/70	N	N	N	22.1	0.74	15.2	9000	74/23/3	1.01	124	39	1.4	130	3	0.8
27	Velu	55yrs	M	79372	18-05-2012	NIL	86	110/70	N	N	N	25.6	1.14	14.3	7800	60/38/2	1.48	112	35	1.2	137	3.5	0.8
28	Gothandam	48yrs	M	77591	18-05-2012	NIL	88	120/80	N	N	N	21.6	0.82	11.2	6550	49/48/3	1.8	119	43	0.9	147	3.8	0.8
29	Rajini	47yrs	M	77586	25-05-2012	NIL	92	90/60	N	N	N	20.6	0.78	15.3	9300	74/23/3	3.3	124	40	1.2	134	3.6	0.9
30	Murugan	50yrs	M	79453	25-05-2012	NIL	84	130/80	N	N	N	18.6	0.7	13.8	7900	68/29/3	3.2	121	27	1	140	4.2	0.6
31	Munnusamy	55yrs	M	79467	25-05-2012	NIL	86	140/90	N	N	N	27.2	1.1	15.2	7600	60/38/2	1.48	107	31	1.2	135	3.8	1
32	Murali	48yrs	M	78570	25-05-2012	NIL	86	130/80	N	N	N	19.4	0.72	13.5	7800	74/24/1	2.5	90	38	1	135	4	0.9
33	Karunakaran	50yrs	M	77591	08-06-2012	NIL	88	120/80	N	N	N	23.5	0.92	14.2	6550	49/48/3	1.8	119	43	0.9	147	3.8	0.8
34	Mohan	48yrs	M	79467	08-06-2012	NIL	86	140/90	N	N	N	23.5	0.96	16	7600	60/38/2	1.48	107	31	1.2	135	3.8	1
35	Munnusamy	48yrs	M	78570	08-06-2012	NIL	86	130/80	N	N	N	24.8	0.94	15.7	7800	74/24/1	2.5	90	38	1	135	4	0.9
36	Ramu	55yrs	M	83467	08-06-2012	NIL	90	120/60	N	N	N	26.6	0.98	15.2	8600	75/23/2	3.6	105	34	1	140	4.5	1
37	Rajendran	50yrs	M	79989	15-06-2012	NIL	78	140/70	N	N	N	24.6	0.94	14.2	5600	65/34/1	1.48	120	44	1.2	132	4	1
38	Chandran	53yrs	M	81556	15-06-2012	NIL	88	130/80	N	N	N	20.2	0.84	13.8	8100	68/29/3	3.5	111	38	0.7	145	3.8	0.7
39	Ponnusamy	55yrs	M	87665	15-06-2012	NIL	84	110/70	N	N	N	23.4	0.92	12.8	7600	60/38/2	1.6	103	32	1	141	4.2	1
40	Mariappan	45yrs	M	89854	15-06-2012	NIL	100	120/80	N	N	N	25.2	1.1	14.3	6970	49/48/3	1.8	90	40	1	145	3.8	0.8
41	Jeyakumar	46yrs	M	89732	22-06-2012	NIL	72	110/70	N	N	N	26.4	1.12	12.5	6230	55/47/3	1.45	125	26	0.7	137	3.1	0.6
42	Sivaguru	50yrs	M	79989	22-06-2012	NIL	78	140/70	N	N	N	29.2	1.2	14.2	5600	65/34/1	1.48	120	44	1.2	132	4	1
43	Seenivasan	50yrs	M	71228	22-06-2012	NIL	72	110/70	N	N	N	30.4	1.18	12.5	9000	74/23/3	1.01	124	39	1.4	130	3	0.8
44	Devarajan	48yrs	M	74510	22-06-2012	NIL	80	110/80	N	N	N	25.6	1.02	13	9600	75/24/1	1.32	94	30	1	135	3.5	1.2
45	Shanmugam	51yrs	M	87665	29-06-2012	NIL	84	110/70	N	N	N	23.6	0.91	15.2	7600	60/38/2	1.6	103	32	1	141	4.2	1
46	Muthukumar	48yrs	M	78570	29-06-2012	NIL	86	130/80	N	N	N	27.8	1.1	16.3	7800	74/24/1	2.5	90	38	1	135	4	0.9
47	Vasu	48yrs	M	95366	29-06-2012	NIL	80	120/80	N	N	N	28.2	1.26	12.8	6110	66/32/2	2.5	110	39	1.1	130	4.2	1
48	Prabhu	42yrs	M	96008	29-06-2012	NIL	88	110/70	N	N	N	24.1	0.9	13	7500	68/30/2	2.4	109	31	0.7	137	3.6	0.7
49	Dhanraj	55yrs	M	94556	06-07-2012	NIL	92	120/80	N	N	N	19.2	0.8	14.3	7800	75/24/1	3	124	28	0.6	138	4.2	0.9
50	Vasu	50yrs	M	71228	06-07-2012	NIL	64	110/70	N	N	N	28.6	1.14	16.2	9000	74/23/3	2.1	124	39	1.4	130	3	0.8
51	Soori	55yrs	M	74510	06-07-2012	NIL	86	110/80	N	N	N	20.4	0.82	13	9600	75/24/1	2.35	94	30	1	135	4.2	1.2
52	Radhakrishnan	53yrs	M	94578	06-07-2012	NIL	74	110/70	N	N	N	19.6	0.76	13.2	7600	70/27/3	3.2	95	38	0.9	140	3.8	0.9
53	Manikkam	55yrs	M	69869	13-07-2012	NIL	88	110/70	N	N	N	20.4	0.82	12.5	6230	65/37/3	2.45	125	26	0.7	137	3.1	0.6
54	Parthasaarathy	54yrs	M	73228	14-07-2012	NIL	92	100/60	N	N	N	20.2	0.82	13.2	7560	72/27/2	2.2	102	40	1	135	4	1.2
55	Anbu	50yrs	M	74882	15-07-2012	NIL	80	120/70	N	N	N	27.2	1.02	14.1	8550	69/29/2	2.7	98	27	1.2	140	3	1
56	Mahesh	51yrs	M	70662	16-07-2012	NIL	92	120/80	N	N	N	21.2	0.9	15.2	7300	65/32/3	2.48	102	31	0.7	132	3.5	0.9
57	Paramasivam	48yrs	M	76025	17-07-2012	NIL	70	100/70	N	N	N	29.1	1.24	15.5	7690	62/36/2	3.2	96	38	1	145	4.3	1
58	Ponnusamy	50yrs	M	72252	18-07-2012	NIL	72	110/60	N	N	N	28.4	1.1	13.6	7580	71/28/1	2.4	114	43	1	141	3.5	0.7
59	Shankar	50yrs	M	76147	19-07-2012	NIL	86	110/80	N	N	N	26.8	0.98	11.3	7856	76/24/0	2.32	106	31	0.7	145	3	0.9
60	Aadi	52yrs	M	72913	20-07-2012	NIL	76	100/60	N	N	N	21.5	0.82	14	8550	72/26/2	2.1	90	38	1.2	137	3.9	0.8
61	Nambi	48yrs	M	74520	21-07-2012	NIL	84	110/80	N	N	N	30.2	1.2	15.2	6655	73/26/1	2.48	120	34	1.4	132	4	1.2
62	Murugan	55yrs	M	71228	22-07-2012	NIL	90	110/70	N	N	N	20.5	0.86	16.2	7900	60/38/2	2.8	116	44	1	130	3.6	0.9

63	Ramachandran	50yrs	M	79378	23-07-2012	NIL	86	110/70	N	N	N	28.8	0.96	14.6	8646	55/42/3	3.3	95	38	1	135	3.7	0.6
64	Chandru	47yrs	M	77590	24-07-2012	NIL	78	120/80	N	N	N	24.2	0.86	15.2	9600	60/37/1	3.2	106	32	1	141	4.7	1
65	Veerasamy	55yrs	M	77486	25-07-2012	NIL	72	90/60	N	N	N	22.6	0.84	14.1	6100	74/24/2	2.48	100	40	1.1	135	3.6	0.9
66	Raja	65yrs	M	79454	26-07-2012	NIL	80	130/80	N	N	N	26.6	0.92	14.3	7560	53/45/3	2.5	118	26	0.7	130	3.5	1
67	Manikam	60yrs	M	79468	27-07-2012	NIL	84	140/90	N	N	N	26.4	0.84	13.2	6876	76/23/1	3.8	96	44	0.6	137	3	1
68	Mannar	58yrs	M	78571	28-07-2012	NIL	86	130/80	N	N	N	23.2	0.84	16	6200	72/25/3	2.48	104	39	1.4	138	3.5	0.7
69	Ramasamy	62yrs	M	77571	29-07-2012	NIL	80	120/80	N	N	N	20.2	0.84	15.8	7600	68/31/1	2.5	122	30	1	130	4	1
70	Kumar	65yrs	M	79469	30-07-2012	NIL	88	140/90	N	N	N	27.2	0.94	13.6	8000	75/23/2	3.6	96	32	0.9	135	3.6	0.8
71	Gajendran	58yrs	M	78575	31-07-2012	NIL	92	130/80	N	N	N	22.1	0.82	12.5	8600	75/24/1	2.48	92	40	0.7	140	3.7	0.6
72	Saminathan	60yrs	M	83477	01-08-2012	NIL	72	120/60	N	N	N	28.6	0.98	15.6	9684	67/30/3	3.5	104	27	1	137	4.7	1
73	Kuppusamy	58yrs	M	79990	02-08-2012	NIL	68	140/70	N	N	N	25.2	0.96	14.9	8800	58/41/1	2.6	99	31	1.2	135	3.6	0.8
74	Kamalakanan	62yrs	M	78450	03-08-2012	NIL	76	130/80	N	N	N	22.6	0.86	16.2	8110	53/45/2	2.6	122	38	0.7	140	3.5	1.2
75	Praveen	65yrs	M	78956	04-08-2012	NIL	92	110/70	N	N	N	25.1	0.9	14.9	8500	60/39/1	2.45	106	43	1	132	3	1
76	Rathinam	60yrs	M	77456	05-08-2012	NIL	84	120/80	N	N	N	27.2	0.96	14	9200	68/32/0	2.48	98	31	1	145	3.5	0.9
77	Swami	62yrs	M	89585	06-08-2012	NIL	90	110/70	N	N	N	29.1	1.1	15.4	6550	65/34/1	2.1	88	38	0.7	141	4	1
78	Rajan	65yrs	M	89562	07-08-2012	NIL	88	120/80	N	N	N	23.1	0.86	13.2	9500	75/23/2	2.32	100	34	1.2	145	4.5	0.7
79	Karupaiya	58yrs	M	78563	08-08-2012	NIL	72	110/70	N	N	N	24.6	0.89	15.4	6850	74/25/1	2.6	120	44	1.4	137	4	0.8
80	Raja	62yrs	M	98563	09-08-2012	NIL	84	130/80	N	N	N	28.2	0.94	15.8	7500	61/38/1	2.5	96	38	1	132	3.8	1.2
81	Murugaiyan	58yrs	M	78456	10-08-2012	NIL	76	120/70	N	N	N	29.4	1.1	14.2	4500	51/46/3	2.5	98	32	1	130	4.2	0.9
82	Nataraj	65yrs	M	89745	11-08-2012	NIL	86	120/80	N	N	N	22.8	0.85	12.8	6750	74/22/4	2.3	104	40	1	135	3.8	0.6
83	Ravi	60yrs	M	68458	12-08-2012	NIL	74	120/80	N	N	N	22.2	0.8	13.6	8900	75/23/2	3	118	26	1.1	141	3.1	1
84	Mahendran	61yrs	M	78498	13-08-2012	NIL	78	90/60	N	N	N	21.6	0.82	15	5200	74/23/3	2.01	94	44	0.7	135	4	0.9
85	Ramkumar	65yrs	M	65265	14-08-2012	NIL	72	120/80	N	N	N	20.6	0.7	16.4	5800	67/31/2	2.32	106	39	0.6	130	3	1
86	Kadhir	62yrs	M	73652	15-08-2012	NIL	80	130/80	N	N	N	26.2	0.98	14.5	5500	56/40/4	3.2	100	30	1.4	137	4.2	1
87	Palani	64yrs	M	74326	16-08-2012	NIL	84	120/80	N	N	N	24.2	0.94	14.6	7500	50/48/2	1.45	120	32	1	138	3.8	0.7
88	Babu	56yrs	M	98231	17-08-2012	NIL	86	100/70	N	N	N	24.6	0.86	16	5000	60/38/2	1.5	115	34	0.9	130	3.1	0.8
89	Saravanan	60yrs	M	98845	18-08-2012	NIL	80	110/80	N	N	N	19.4	0.78	15.4	5500	68/31/1	2.3	112	44	0.7	135	4	0.6
90	Durai	58yrs	M	81258	19-08-2012	NIL	88	100/60	N	N	N	30.6	1.15	14.6	5700	65/35/0	2.5	100	38	1	140	3	1
91	Kannan	68yrs	M	86523	20-08-2012	NIL	92	130/90	N	N	N	20.1	0.84	13.5	7800	75/24/1	2.5	96	32	1	137	3.8	0.8
92	Selvam	70yrs	M	89897	21-08-2012	NIL	66	120/90	N	N	N	26.1	0.96	16.4	8700	74/23/3	2	104	40	1.1	135	4.2	1.2
93	Vignesh	70yrs	M	85276	22-08-2012	NIL	86	130/90	N	N	N	22.6	0.92	15.4	6750	60/38/2	3	120	26	0.7	130	3.8	1
94	Aravind	72yrs	M	77498	23-08-2012	NIL	88	130/80	N	N	N	20.5	0.86	13.2	9850	49/48/3	2.36	122	44	0.6	137	3.1	0.9
95	Balasekar	68yrs	M	69565	24-08-2012	NIL	80	120/90	N	N	N	22.4	0.82	14.2	4500	74/23/3	2.32	108	39	1.4	138	4	1
96	Kesavan	66yrs	M	89137	25-08-2012	NIL	86	110/70	N	N	N	20.2	0.78	16.2	4300	68/29/3	3.2	96	30	1	130	3	0.7
97	Perumal	68yrs	M	79135	26-08-2012	NIL	72	120/80	N	N	N	26.5	0.94	13	6500	49/48/3	2.4	100	32	0.9	135	3.8	0.8
98	Prasanth	70yrs	M	84625	27-08-2012	NIL	76	130/90	N	N	N	20.2	0.84	14.6	7400	74/23/3	3.2	114	30	1	140	4.2	0.9
99	Varatharajan	72yrs	M	96325	28-08-2012	NIL	90	120/90	N	N	N	22.5	0.92	16.4	8500	68/29/3	2.45	120	32	0.9	137	3.8	1
100	Sridhar	70yrs	M	74125	29-08-2012	NIL	86	110/70	N	N	N	19.6	0.82	17.4	7530	69/28/3	2.56	118	34	0.8	136	3.9	0.8

LFT				HIV	OT CHOLESTROL(mg/d	Serum Total TESTOSTERONE (ng/dl)
DB (mg/dl)	OT (IU/L)	PT (IU/L)	TP (g/dl)			
0.3	28	20	6.5	negative	182	820
0.3	20	32	6.2	negative	184	614
0.4	25	38	6.4	negative	176	812
0.2	28	20	5.4	negative	190	616
0.4	25	39	7	negative	230	450
0.4	21	22	5.8	negative	186	712
0.2	24	36	6.2	negative	180	720
0.2	29	31	5.8	negative	190	720
0.3	24	28	6.2	negative	186	840
0.4	28	36	6.2	negative	184	820
0.3	28	32	7	negative	200	740
0.4	24	36	6.9	negative	198	550
0.4	24	29	6.2	negative	220	470
0.2	27	32	5.8	negative	184	680
0.2	28	32	6.4	negative	216	720
0.2	23	30	6.8	negative	236	813
0.4	28	32	7	negative	186	720
0.3	23	20	7	negative	180	720
0.2	32	20	6.7	negative	188	728
0.2	31	21	7	negative	226	440
0.2	25	38	6.2	negative	184	685
0.2	28	32	6.8	negative	210	520
0.3	27	22	6.6	negative	186	572
0.3	28	16	6.4	negative	206	510
0.3	27	22	7	negative	200	620
0.3	23	23	7	negative	188	710
0.2	32	20	6.8	negative	206	670
0.2	28	30	6.2	negative	190	770
0.3	29	34	6.6	negative	186	620
0.1	20	32	6.1	negative	186	720
0.3	28	36	6.2	negative	200	690
0.3	30	28	7	negative	178	612
0.2	28	30	6.2	negative	186	640
0.3	28	36	6.2	negative	180	714
0.3	30	28	7	negative	182	780
0.2	24	36	6	negative	194	609
0.3	28	30	6.5	negative	198	780
0.2	24	28	5.8	negative	196	790
0.3	28	30	6.5	negative	192	610
0.2	26	30	7.2	negative	200	550
0.1	28	16	6.2	negative	196	606
0.3	28	30	6.5	negative	216	590
0.3	23	25	7	negative	230	520
0.3	27	18	7	negative	190	510
0.3	28	30	6.5	negative	192	580
0.3	30	28	7	negative	196	620
0.3	22	35	6.8	negative	220	701
0.2	22	27	6.2	negative	210	554
0.2	28	36	6.5	negative	180	720
0.3	23	20	7	negative	200	750
0.3	27	22	7	negative	186	660
0.2	21	27	6.6	negative	180	624
0.1	28	16	6.2	negative	188	740
0.2	30	20	6.8	negative	184	640
0.3	30	32	6.2	negative	210	560
0.2	16	38	6.6	negative	180	614
0.3	30	20	6.1	negative	232	468
0.2	24	39	6.2	negative	200	565
0.1	42	22	7	negative	196	580
0.3	30	36	6.2	negative	184	620
0.3	28	31	6.2	negative	230	562
0.3	35	28	7	negative	184	670

0.3	27	32	6	negative	224	420
0.3	36	36	6.5	negative	196	620
0.3	20	28	5.8	negative	188	640
0.2	22	30	6.5	negative	210	482
0.2	27	36	7.2	negative	200	620
0.3	16	28	6.2	negative	184	562
0.3	30	36	6.5	negative	180	710
0.2	16	30	7	negative	230	487
0.3	30	28	7	negative	182	580
0.3	25	30	6.5	negative	210	670
0.3	18	30	7	negative	198	520
0.3	30	16	6.8	negative	188	560
0.2	28	30	5.8	negative	200	510
0.2	35	28	6.5	negative	206	540
0.3	27	28	7.2	negative	224	639
0.1	36	30	6.2	negative	198	580
0.3	20	24	6.5	negative	180	550
0.3	22	28	7	negative	212	480
0.2	27	24	6.5	negative	220	510
0.3	16	28	7	negative	186	610
0.3	23	26	6.8	negative	190	580
0.2	32	28	6.2	negative	184	610
0.3	28	28	6.8	negative	180	540
0.3	29	23	6.2	negative	200	510
0.3	20	23	6.6	negative	196	585
0.3	28	32	6.1	negative	189	582
0.2	30	28	6.2	negative	182	610
0.2	28	29	7.2	negative	236	720
0.3	28	20	6.2	negative	186	462
0.1	30	28	6.5	negative	204	302
0.3	24	30	7	negative	198	460
0.3	28	28	6.5	negative	190	570
0.2	24	23	7	negative	194	480
0.3	28	27	6.5	negative	180	528
0.3	29	28	7.2	negative	200	370
0.2	20	30	6.2	negative	192	598
0.3	28	23	6.5	negative	180	465
0.3	19	21	7.5	negative	186	475

DISSERTATION ON

STUDY OF TESTOSTERONE LEVELS IN MEN WITH TYPE 2 DIABETES MELLITUS

Submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the regulations

for the award of the degree of

M.D. BRANCH - I

GENERAL MEDICINE

MADRAS

CHENGALPATTU MEDICAL COLLEGE AND GOVERNMENT

GENERAL HOSPITAL, CHENGALPATTU

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

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Assignment title	Medical
Author	Asir Julin 20101401 M.D. General Medicine
E-mail	asir_julin@yahoo.in
Submission time	16-Dec-2012 01:58PM
Total words	11728

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DISSERTATION ON STUDY OF TESTOSTERONE LEVELS IN MEN WITH TYPE 2 DIABETES MELLITUS Submitted to THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY In partial fulfilment of the regulations for the award of the degree of M.D. BRANCH - I GENERAL MEDICINE MADRAS CHENGALPATTU MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL, CHENGALPATTU THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI, INDIA APRIL 2013 INTRODUCTION Testosterone a 19-carbon steroid secreted by the testis (Leydig cells) is the primary circulating androgen in the male human. Testosterone is essential for health and well- being and its levels decreases with aging. Men with type 2 diabetes mellitus have low testosterone levels, but this...

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Dated:20.06.2012.

Sub: Medical Education – Chengalpattu Medical College, Chengalpattu – Dr.P.Asir Julin, Post Graduate Student in M.D.(General Medicine) – Admitted during the Academic year 2010-2011 – Dissertation submitted for the Approval of the Human Ethical Committee for the study work entitled **"Serum Testosterone Levels in Men with Type 2 Diabetes Mellitus" - Approved - Orders - Issued.**

Ref: 1) Application dated: 27.03.2012f the Individual.
2) Letter dated 27.03.2012 of the Head of the Department of General Medicine, Chengalpattu Medical College,Chengalpattu.

...

Dr.P.Asir Julin, Post Graduate Student in M.D.(General Medicine) of this college has submitted a Dissertation for the study work entitled "Serum Testosterone Levels in Men with Type 2 Diabetes Mellitus . The Study of the above individual has been approved by the Human Ethical Committee of the Chengalpattu Medical College, Chengalpattu which is forwarded herewith for further course of action.

Further, as per the Regulations of the Tamil Nadu Dr.M.G.R.Medical University, Chennai – 32 with regard to submission of 4 **Copies of Dissertation** with C.D.(2 copies) for the Post Graduate Degree Course, the Dissertation shall be a bound volume of minimum 50 pages and not exceeding 75 pages of typed matter (Double line spacing and one side only) excluding Certification, acknowledgement, annexure and Bibliography". The name of the candidate should not be found anywhere in the Dissertation except in the Certificate. The Dissertation should be forwarded through the Unit Chief/H.O.D./Head of the Institution as per the Colour **(LIGHT GREEN)** as communicated by the University.

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Asir 6/20/12

Encl.: Copy of the Dissertation Study Work.

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Dr.P.Asir Julin,,
P.G.Student in M.D.(General Medicine),
Chengalpattu Medical College, Chengalpattu. .. through the H.O.D. of General Medicine.

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4)ME II Section through the Office Superintendent (ME).
5)PG Admission file 2010-2011.